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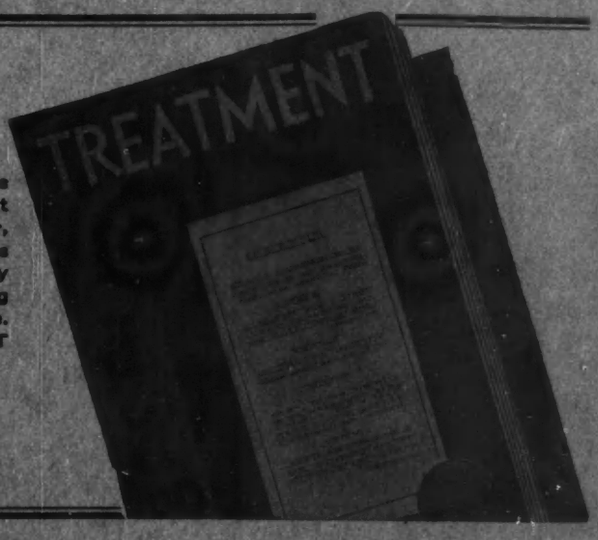

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The Canadian
Medical Association Journal

Vol. 37 TORONTO, JULY, 1937 No. 1

THE PREVENTION OF SILICOSIS BY METALLIC ALUMINUM*

I. A PRELIMINARY REPORT

BY J. J. DENNY, M.Sc., *Metallurgical Engineer,*
W. D. ROBSON, M.B., *Chief Surgeon, McIntyre Mine, Schumacher, Ont.,*
DUDLEY A. IRWIN, M.B., *Associate Professor, Department of Medical Research, University of Toronto*

IN November, 1932, an investigation of silicosis was undertaken at the McIntyre Porcupine Mine, Schumacher, Ont., after a discussion of the problem with Sir Frederick Banting and his staff. As a result it was decided to carry on dusting experiments with animals at the mine in a manner that would duplicate as far as possible actual industrial conditions. At that time 50 guinea pigs were placed in the crusher house tunnel of the mill where a considerable quantity of fine dust, containing approximately 35 per cent of free silica, was being constantly produced. These animals lived in this atmosphere for periods up to one year, and, while on autopsy large amounts of dust were found in the lungs, not a single case of silicosis had developed. These negative results suggested, among other things, that the mine gases might be a predisposing factor in the production of silicosis, and the results of this investigation[1] led us to undertake the study of the hydrogen-ion concentration of the condensate of the atmosphere, both in the mine and in various sections of the mill. The CO_2 combining power of blood serum on a series of 400 miners was also studied at this time. While these results were inconclusive, the variation in the hydrogen-ion concentration of the condensate between the surface and underground atmospheres encouraged us to investigate the effect of neutral, weak acid and alkaline solutions on the solubility of silicious materials.

Gye and Purdy[2] were the first to point out that the chemical reaction and not the physical presence of silicious material was responsible for the production of the fibrosis in silicosis. This work was investigated by Gardner and Cummings,[3] who showed that the tissue reaction to quartz was definitely proportional to the size of the particle. They found that 1-3 micron particles of quartz produced an acute proliferative fibrotic response, while the 10-12 micron particles produced only a foreign body reaction up to a period of three years. It is accepted that the dangerous silica particles retained by the lung are under 5 microns in diameter. We assumed that if the solubility of the silicious material retained in the lung could be reduced sufficiently by the addition of some non-toxic element or compound the usual fibrotic response would be modified. We found that the addition of certain compounds to silica would reduce its solubility in the beaker to a slight extent. But these compounds, when mixed with quartz, injected subcutaneously or inhaled, did not lessen or else actually increased the tissue response produced by quartz alone. Some of these compounds were found to be toxic.

Various elements and compounds were then investigated, and on March 4, 1936, two of us (D. and R.) discovered at the McIntyre Mine that the presence of small amounts of metallic aluminum almost completely prevented silicious material from passing into solution. This discovery was made after investigating Heffernan's[4] theory, which was based on the work of Bragg.[5]

* As presented before the Academy of Medicine, Toronto, June 15, 1937.

Heffernan suggests that silica is active when freshly fractured because of its molecular structure, which presents numerous unsatisfied oxygen atoms to interact with tissue elements. This suggested to us that if the unsatisfied oxygen atoms could be satisfied with nascent hydrogen it might diminish the toxicity of silica in tissue and change a fibrotic response into a simple foreign body reaction.

Animal experimentation was commenced on June 10, 1936, dusting a group of rabbits with mine quartz, to which small quantities of metallic aluminum had been added. In this experiment 13 rabbits were dusted in specially constructed chambers. Six control animals were dusted with quartz alone, while 7 were dusted with quartz plus less than 1 per cent of metallic aluminum. At various intervals up to six months, the lungs and other organs of the animals were sent to one of us (I.) for pathological examination. On sectioning it was found that all the controls showed a picture varying from early to well established silicosis, depending on the length of exposure. The animals subjected to silica dust containing metallic aluminum all showed either minimal or no fibrosis of the lungs. No damage was seen in the lungs or other organs that could be attributed to the presence of aluminum. These results showed that silicosis was inhibited in this small group of rabbits by the admixture of *less than 1 per cent* of metallic aluminum to the quartz dust.

Dusting experiments similar to the one described above are being carried on at the present time, using larger groups of animals. From this group, following 3½ months' dusting, the lungs of one quartz control and two quartz and aluminum dusted animals were sectioned. The lungs of the control animal showed beginning silicosis, while the two animals dusted with quartz and *1 per cent aluminum* showed *no evidence of any fibrosis.*

I. Experimental Work

(*a*) Chemical

*Silicious materials used for solubility tests**.*—Samples of quartz were obtained from Porcupine, Kirkland Lake and Sudbury mining districts in Ontario and from South Africa. Samples of chert and quartzite were obtained from British Columbia. Gray Vermont, Georgia and Ontario granites and a red Ontario granite were collected. Samples of flint and various silicates were obtained. Some samples were reduced to a fine powder by grinding dry in a steel mortar, others (quartz) in a quartz-lined tumble box, to avoid contamination as much as possible. The quartz, flint, chert and quartzite powders were all –325 mesh, microscopic examination showing that over half of the material was composed of particles under 5 microns in their greatest diameter. The silicates were –100 mesh, but contained many fine particles.

Metallic aluminum powder.—Various grades of aluminum powder were tested. It was found that the activity of the aluminum depended upon its state of division and purity, (Table I).

Table I.

Effect of Aluminum Fineness on the Solubility of Quartz

	Dissolved SiO_2 p.p.m.	*Percentage Reduction*
100 c.c. H_2O + 1.0 gm. McIntyre Quartz –325 mesh	50.0	–
100 c.c. H_2O + 1.0 gm. McIntyre Quartz + 1 mg. coarse Al	9.2	82
100 c.c. H_2O + 1.0 gm. McIntyre Quartz + 1 mg. medium Al	2.2	95
100 c.c. H_2O + 1.0 gm. McIntyre Quartz + 1 mg. fine Al	1.9	96

Ether-washed metallic aluminum powder was separated into three fractions by air separation.

Solubilities were determined in Pyrex flasks with continuous agitation.

Time—17 hours.

Temperature—40 to 50° C.

The sample that proved to be most satisfactory contained 99 per cent metallic aluminum and was –20 microns. The usual coating used in the manufacture of metallic aluminum powder was removed by washing with ether. This procedure was found to be imperative.

The solubility tests were done routinely in rubber-stoppered Bakelite tubes, but platinum and pyrex glass containers were also used. The concentration of the silicate ion was determined colorimetrically by the method of King and Dolan.[6, 7] This method was used routinely after it was found to check with gravimetric determinations.

We found that certain types of silica sand (*e.g.*, Montreal silica) were less soluble than naturally occurring quartz. This led to a complete analysis of mine quartz, which was found to contain 85 to 98 per cent silica with 2 to 15

* The term "solubility" is used to indicate the concentration of silica in solution obtained under the conditions as noted.

per cent impurities, the bulk of which were alkaline earth carbonates, (Table II). The addition of small amounts of these alkaline carbonates, or the hydroxides of Na, Ca, etc., added to the silica sand increased its solubility as shown in Tables III and IV. When the impurities of mine quartz were removed by leaching with hydrochloric acid, the solubility was comparable to that of the Montreal sand, (Chart 1). It is also shown in Chart 1 that the presence of metallic aluminum reduces the solubility of naturally occurring quartz to less than that of acid treated quartz.

TABLE II.

ANALYSIS OF MONTREAL SILICA AND MCINTYRE QUARTZ*

Percentage	*Montreal Silica Sand*	*McIntyre Quartz*
SiO_2	99.6	98.1
Fe_2O_3	0.02	0.20
Al_2O_3	0.19	0.42
CaO	None	0.34
MgO	Trace	0.12

PETROGRAPHIC ANALYSIS

Montreal Silica Sand.—"This sample is essentially composed of angular quartz grains. There is, however, some percentage of impurities present. Unlike the other sample these impurities are included in the quartz. They are mostly gas globules and minute hair-like crystals of rutile. There are other impurities but they are not prominent."

McIntyre Quartz.—"This sample is composed essentially of angular quartz grains. There is, however, at least 5 per cent of impurities present. These impurities are mostly ankerite and sericite. Chlorite and pyrite are not so prominent. These impurities are admixed and not present as inclusions in the quartz."

TABLE IIIa.

EFFECT OF INCREASING CONCENTRATIONS OF CALCIUM CARBONATE ON THE SOLUBILITY OF MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
100 c.c. H_2O + 1 gm. Montreal Silica Sand –325 mesh	3.8	6.8
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 5 mg. $CaCO_3$ (0.5%)	12.3	7.1
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 20 mg. $CaCO_3$ (2.0%)	12.1	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 53 mg. $CaCO_3$ (5.3%)	12.9	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 111 mg. $CaCO_3$ (11.1%)	12.2	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 250 mg. $CaCO_3$ (25.0%)	12.4	7.8
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. ankerite (1.0%)	6.9	
100 c.c. H_2O + 1 gm. $CaCO_3$ (blank)	Trace	

Time—24 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

* We are indebted for the above petrographic analysis to Dr. Eugene Poitevin, Chief, Section of Mineralogy, Department of Mines, Ottawa.

TABLE IIIb.

EFFECT OF CONSTANT METALLIC ALUMINUM AND VARYING CALCIUM CARBONATE CONCENTRATIONS ON MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
100 c.c. H_2O + 1 gm. Montreal Silica Sand –325 mesh + 10 mg. Al	0.5	6.9
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 5 mg. $CaCO_3$	0.5	7.1
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 53 mg. $CaCO_3$	0.5	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 250 mg. $CaCO_3$	0.5	7.8
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 1.0 mg. $CaCO_3$	0.5	–

Time—12 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

TABLE IIIc.

EFFECT OF VARYING CONCENTRATIONS OF CALCIUM HYDROXIDE ON THE SOLUBILITY OF MCINTYRE QUARTZ AND MONTREAL SILICA SAND

	$Ca(OH)_2$ mg.	*Dissolved SiO_2 p.p.m.*	*pH*
1 gm. McIntyre Quartz –325 mesh + 100 c.c. H_2O	0	27.1	7.0
1 gm. McIntyre Quartz + 100 c.c. 0.006% $Ca(OH)_2$ solution	6	56.0	9.3
1 gm. McIntyre Quartz + 100 c.c. 0.064% $Ca(OH)_2$ solution	64	2.7	12.2
1 gm. McIntyre Quartz + 100 c.c. 0.127% $Ca(OH)_2$ solution	127	0.6	12.4
1 gm. Montreal Silica Sand –325 mesh + c.c. H_2O	0	3.0	6.8
1 gm. Montreal Silica Sand + 100 c.c. 0.006% $Ca(OH)_2$ solution	6	25.2	9.5
1 gm. Montreal Silica Sand + 100 c.c. 0.064% $Ca(OH)_2$ solution	64	2.5	12.2
1 gm. Montreal Silica Sand + 100 c.c. 0.127% $Ca(OH)_2$ solution	127	0.6	12.4
100 c.c. 0.127% $Ca(OH)_2$ solution (blank)	127	0.3	12.4

Time—20 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

$Ca(OH)_2$ solution prepared by igniting Bakers C.P. Calcium Carbonate, dissolving in water and filtering. The strength was determined by titration with HCl.

TABLE IIId.

EFFECT OF PORTLAND CEMENT ON THE SOLUBILITY OF MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
100 c.c. H_2O + 1 gm. Montreal Silica Sand –325 mesh	2.0	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 20 mg. cement	41.2	–
100 c.c. H_2O + 20 mg. cement (blank)	23.4	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 1.0 gm. cement	1.0	12.4

Time—20 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

The effect of varying amounts of metallic aluminum powder on the solubility of quartz was determined (Chart 2). The solubility of flint and quartz from other localities was found to be comparable to that of McIntyre quartz, and was reduced to the same extent on the addition of metallic aluminum. Various other samples of quartz, quartzite and chert were found to react in a similar manner (Table V).

A number of silicates were then tested with results as tabulated in Table VI.

TABLE IV.

EFFECT OF SODIUM CARBONATE AND SODIUM HYDROXIDE ON THE SOLUBILITY OF MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
1.0 gm. Montreal Silica Sand –325 mesh + 100 c.c. H_2O	2.7	6.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.006% NaOH solution	12.9	11.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.06% NaOH solution	60.9	12.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.13% NaOH solution	64.2	12.4
100 c.c. NaOH solution 0.13% (blank)	0.6	12.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.006% Na_2CO_3 solution	8.7	8.8
1.0 gm. Montreal Silica Sand + 100 c.c. 0.06% Na_2CO_3 solution	21.7	11.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.13% Na_2CO_3 solution	21.0	11.8
100 c.c. Na_2CO_3 solution 0.13% (blank)	0.6	11.8

Time—20 hours.

Temperature—37° C.

All tests conducted in Bakelite tubes with continuous agitation.

TABLE V.

EFFECT OF METALLIC ALUMINUM POWDER ON THE SOLUBILITY OF QUARTZ DUST

Dust	*pH*	*Dissolved SiO_2 p.p.m.*	*Percentage Reduction*
Blank	7.0	0.3	–
P 2	7.0	17.7	
P 2 + Al	7.0	0.7	96
P 3	7.0	17.3	
P 3 + Al	7.1	1.0	94
P 4	7.0	24.0	
P 4 + Al	7.0	0.8	97
P 5	7.0	22.6	
P 5 + Al	7.0	0.6	97
P 6	7.0	13.7	
P 6 + Al	7.0	0.8	94
P 7	7.1	15.4	
P 7 + Al	7.1	0.9	94
P 8	7.0	14.0	
P 8 + Al	7.1	1.3	91
K 4	7.0	14.5	
K 4 + Al	7.1	0.9	94
K 5	7.1	16.8	
K 5 + Al	7.1	0.7	96
K 7	7.1	19.3	
K 7 + Al	7.0	1.5	92
S 1	6.9	21.5	
S 1 + Al	6.9	1.2	95
Kolar Quartz	7.1	28.2	
Kolar Quartz + Al	7.2	1.8	94
South African Banket	7.1	8.8	
South African Banket + Al	7.1	1.8	80
Chert	6.8	22.1	
Chert + Al	6.8	5.0	78
Quartzite	6.8	17.9	
Quartzite + Al	6.8	5.7	69
Flint	7.0	147.0	
Flint + Al	7.0	3.4	97.7

Dust used—1.0 gram.
Aluminum used—10 mg.
H_2O used—50 c.c.
Time—48 hours.
Temperature—37° C.
P—indicates Porcupine Quartz.
K—indicates Kirkland Lake Quartz.
S—indicates Sudbury Quartz.
All tests conducted in Bakelite tubes with continuous agitation at 20 r.p.m.

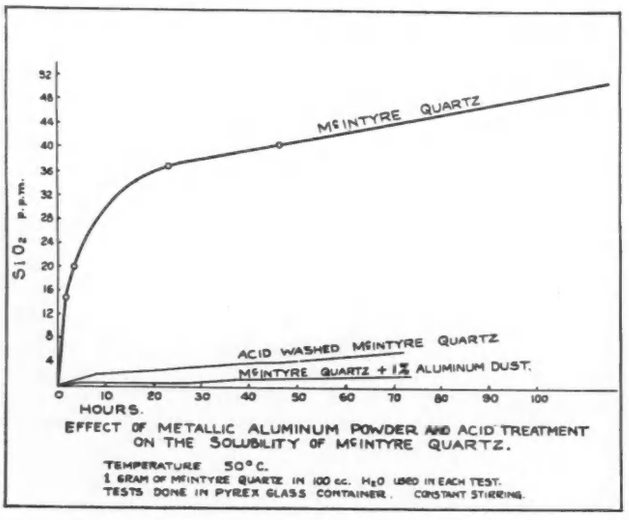
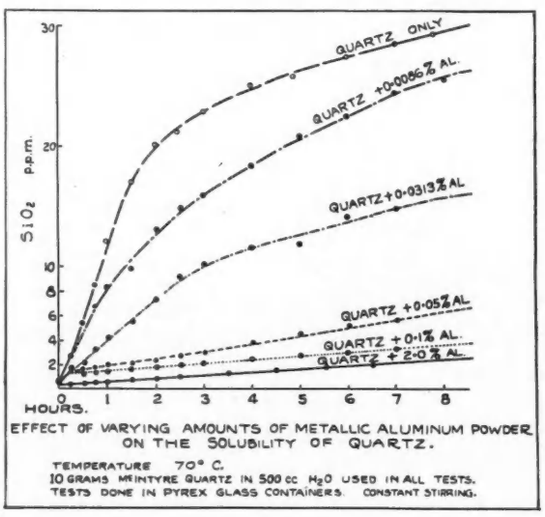

McINTYRE QUARTZ
ACID WASHED McINTYRE QUARTZ
McINTYRE QUARTZ + 1% ALUMINUM DUST.
SiO2 p.p.m.
HOURS.
EFFECT OF METALLIC ALUMINUM POWDER AND ACID TREATMENT ON THE SOLUBILITY OF McINTYRE QUARTZ.
TEMPERATURE 50° C.
1 GRAM OF McINTYRE QUARTZ IN 100 cc. H2O USED IN EACH TEST.
TESTS DONE IN PYREX GLASS CONTAINER. CONSTANT STIRRING.

Chart 1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QUARTZ+0·0313% AL
QUARTZ +0·05% AL.
QUARTZ +0·1% AL.
QUARTZ + 2·0 % AL.
SiO2 p.p.m.
HOURS.
EFFECT OF VARYING AMOUNTS OF METALLIC ALUMINUM POWDER ON THE SOLUBILITY OF QUARTZ.
TEMPERATURE 70° C.
10 GRAMS McINTYRE QUARTZ IN 500 cc H2O USED IN ALL TESTS.
TESTS DONE IN PYREX GLASS CONTAINERS. CONSTANT STIRRING.

Chart 2

TABLE VI.

EFFECT OF METALLIC ALUMINUM ON THE SOLUBILITY OF SILICATES

	pH	*Dissolved SiO_2 p.p.m.*	*Percentage Reduction*
1.0 gm. dust P 14 + 50 c.c. H_2O	7.0	12.4	
" " dust P 14 + 50 c.c. H_2O + 10 mg. Al	7.0	0.7	94
1.0 gm. dust P 15 + 50 c.c. H_2O	7.2	6.1	
" " dust P 15 + 50 c.c. H_2O + 10 mg. Al	7.2	1.9	69
1.0 gm. asbestos + 50 c.c. H_2O	6.9	21.2	
" " asbestos + 50 c.c. H_2O + 10 mg. Al	7.0	0.8	96
1.0 gm. serpentine + 50 c.c. H_2O	7.1	10.0	
" " serpentine + 50 c.c. H_2O + 10 mg. Al	7.1	0.9	91
1.0 gm. talc + 50 c.c. H_2O	7.2	64.0	
" " talc + 50 c.c. H_2O + 10 mg. Al	7.1	1.0	98
1.0 gm. sericite + 50 c.c. H_2O	7.0	40.7	
" " sericite + 50 c.c. H_2O + 10 mg. Al	7.1	0.9	98
1.0 gm. oligoclase + 50 c.c. H_2O	7.0	7.6	
" " oligoclase + 50 c.c. H_2O + 10 mg. Al	7.0	0.4	95
1.0 gm. albite + 50 c.c. H_2O	7.0	7.6	
" " albite + 50 c.c. H_2O + 10 mg. Al	7.0	0.7	91
1.0 gm. orthoclase + 50 c.c. H_2O	6.9	7.1	
" " orthoclase + 50 c.c. H_2O + 10 mg. Al	7.0	0.5	93
1.0 gm. microcline + 50 c.c. H_2O	7.0	8.0	
" " microcline + 50 c.c. H_2O + 10 mg. Al	7.0	1.0	87
1.0 gm. wollastonite + 50 c.c. H_2O	7.4	27.2	
" " wollastonite + 50 c.c. H_2O + 10 mg. Al	7.2	0.8	97
1.0 gm. kaolin + 50 c.c. H_2O	6.8	6.2	
" " kaolin + 50 c.c. H_2O + 10 mg. Al	6.8	0.7	89
1.0 gm. labradorite + 50 c.c. H_2O	6.9	7.6	
" " labradorite + 50 c.c. H_2O + 10 mg. Al	6.9	0.5	93
1.0 gm. Canadian Grey Granite + 50 c.c. H_2O	6.9	6.4	
" " Canadian Grey Granite + 50 c.c. H_2O + 10 mg. Al	7.0	0.7	89
1.0 gm. Canadian Red Granite + 50 c.c. H_2O	7.0	6.7	
" " Canadian Red Granite + 50 c.c. H_2O + 10 mg. Al.	7.0	0.8	88
1.0 gm. Georgia Granite + 50 c.c. H_2O	7.0	7.7	
" " Georgia Granite + 50 c.c. H_2O + 10 mg. Al	7.0	0.8	90
1.0 gm. Vermont Granite + 50 c.c. H_2O	7.0	6.9	
" " Vermont Granite + 50 c.c. H_2O + 10 mg. Al	7.0	1.0	85

P 14—McIntyre Mine underground aerial dust.
P 15—McIntyre Mine surface crusher house aerial dust.
Time—48 hours.
Temperature—37.5° C.
All tests conducted in Bakelite tubes with continuous agitation.

TABLE VII.

COMPARISON OF VARIOUS FORMS OF ALUMINUM COMPOUNDS WHEN USED TO REDUCE THE SOLUBILITY OF SILICA

	Dissolved SiO_2 p.p.m.	*Percentage Reduction*
1 gm. McIntyre Quartz –325 mesh + 100 c.c. H_2O	35	–
1 gm. McIntyre Quartz + 100 c.c. H_2O + 10 mg. Al dust	0.3	99
1 gm. McIntyre Quartz + 100 c.c. H_2O + 29 mg. $Al(OH)_3$ (freshly pp't'd.)	2.8	92
1 gm. McIntyre Quartz + 100 c.c. H_2O + 29 mg. $Al(OH)_3$ (commercial product C.P.)	20.7	41
1 gm. McIntyre Quartz + 100 c.c. H_2O + 19 mg. Al_2O_3	1.8	95
1 gm. McIntyre Quartz + 100 c.c. H_2O + 29 mg. Bauxite	17.3	51
1 gm. McIntyre Quartz + 100 c.c. H_2O + 100 mg. Bauxite	4.3	88

Time—48 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

(*b*) DUSTING EXPERIMENTS

These experiments were planned with two fundamental principles in mind (*a*) to duplicate as far as possible the dust produced underground by blasting, (*i.e.*, freshly fractured, finely particulate dust particles, relatively dry); (*b*) to avoid as much as possible any contamination in the dust produced.

Method of experimental dusting.—Galvanized iron drums (Fig. 1), 31″ long and 22″ in diameter were used as dusting chambers. In the upper portion of each drum a tumbling box was installed. These boxes were constructed of ½″ oak and measured 7″ x 7″ x 26″ outside diameter. The boxes were lined with quartz slabs, ½″ to 1″ in thickness, which were keyed in position, leaving an inside space about 4″ x 4″ x 23″. This space was half filled with lump quartz, varying in size from ½″ to 1″ in

diameter. These boxes were driven by a 1/6 h.p. motor, and revolved at a speed of 60 r.p.m. The dust produced escaped through twenty-four 3/16″ holes drilled through each face of the box. The drums were ventilated by a positive pressure at a rate of 2.5 cu. ft. per minute, which was sufficient to maintain the CO_2 content of the drum below 0.3 per cent during the dusting of the animals. One end of the drum was fitted with a removable cover, 16″ in diameter, containing a glass window and a rubber port for air sampling. This cover provided access to the interior of the drum.

Four drums were constructed as described above. Each tumbling box contained about 10 lbs. of loose quartz as a grinding medium. Box No. 1 produced quartz dust alone. To each of boxes 2, 3 and 4 was added 100 gm. of aluminum pellets approximately ¼″ in diameter, to produce a mixed quartz and aluminum dust. The dust produced by these boxes was found by chemical analysis to contain less than 1 per cent metallic aluminum by weight. Solubility tests were made on the dust collected from a shelf in each drum at intervals.

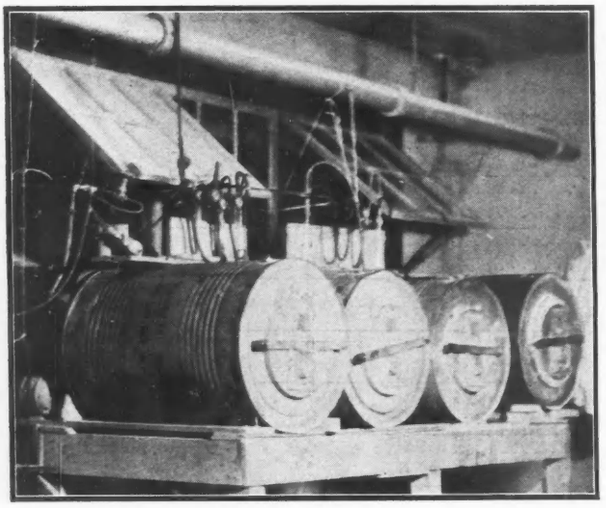

Fig. 1.—Photograph of drums used in dusting experiments.

Sample.—Continuous agitation in Bakelite tubes for 20 hours at 40° C.

	Dissolved SiO_2 p.p.m.	*Percentage Reduction*
Drum 1—Quartz only	76.3	..
Drum 2—Quartz plus Al ..	2.5	97
Drum 3—Quartz plus Al ..	2.4	97
Drum 4—Quartz plus Al ..	3.1	96

Four rabbits were placed in each drum for dust exposure from 12 to 16 hours daily.

During the period of dusting, konimeter counts were taken daily. The dust counts varied from 4,000 to 8,000 particles per c.c. Microscopic examination of the dust showed it to be very finely particulate, about 90 per cent of the particles being under 5 microns in diameter. When the konimeter counts fell below 4,000 particles per c.c., the tumbling box was replaced by one freshly loaded.

PATHOLOGICAL FINDINGS

The duration of the experimental dust exposure and the amount of silica found on chemical analysis in the lung tissue is given in Table VIII, for 6 rabbits dusted with quartz alone and 7 rabbits dusted with quartz and aluminum ground together.

TABLE VIII.
TYPE AND DURATION OF DUST EXPOSURE AND SILICA ASSAY OF LUNGS OF RABBITS

Rabbit No.	*Type of dust*	*Dusting history Hours daily*	*Duration weeks*	*Lung SiO_2 mg. per 100 grams dry weight*
105	Quartz	12	20	2350
99	"	16	24	8140
104	"	14	24	4280
102	"	16	24	6260
91	"	16	37	1850
62	"	16	36	3610
100	" + Al ...	16	20	6780
98	" " ...	16	20	8230
97	" " ...	16	20	5700
95	" " ...	16	21	8730
94	" " ...	16	21	2700
96	" " ...	16	24	7780
93	" " ...	16	24	9200

The lungs of these animals were removed intact and gently distended by the intra-tracheal injection of 10 per cent formo-saline prior to immersion in the same fixative. As a routine, tissue blocks cut from the two upper and lower lobes of each lung and from the mediastinal lymphatic glands were dehydrated in alcohols of ascending concentration, cleared in xylol, and imbedded and cut in paraffin. The sections were mounted serially in sets of three; the first was incinerated, the second was stained with hæmatoxylin and eosin, the third was incinerated and treated with hydrochloric acid. Tissue blocks from the liver, spleen and kidneys were fixed, sectioned and stained in a similar manner.

Gross appearance of the lungs.—The lungs of all the quartz-dusted animals presented an appearance that was fairly uniform. Subpleural collections of dust were scattered over the surface of the lung. These areas were light in colour and varied in size from 1 to 5 mm. The cut surface of the lungs showed

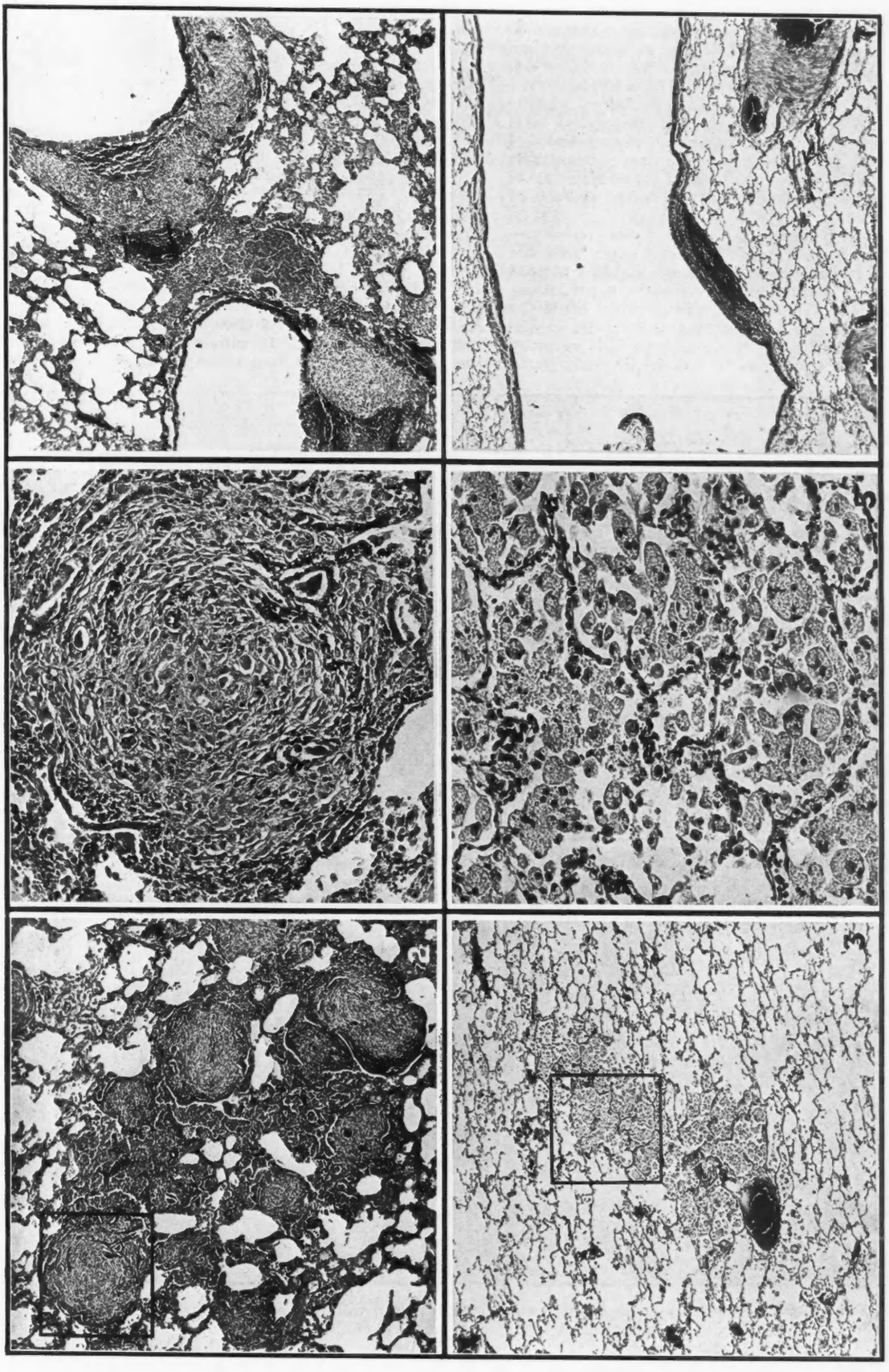

Fig. 2.—Proliferative response with fibrotic nodule formation produced in the lung of a rabbit dusted 16 hours daily for 6 months with quartz.
Fig. 3.—Foreign body response produced in the lung of a rabbit dusted 16 hours daily for 6 months with quartz and aluminum. **Fig. 4.**—Higher magnification of marked area in Fig. 2. **Fig. 5.**—Higher magnification of marked area in Fig. 3. **Fig. 6.**—Fibrotic areas in peribronchial lymphatic aggregations of a rabbit dusted with quartz 16 hours daily for 6 months. **Fig. 7.**—Peribronchial lymphatic aggregations of a rabbit dusted with quartz and aluminum 16 hours daily for 6 months, for comparison with Fig. 6.

numerous small grayish firm nodules scattered throughout. Some of these nodules were discrete, while others were surrounded by halos of condensation. The mediastinal lymphatic glands, usually 2 or 3 in number, were firm and enlarged to several times their normal size.

The lungs of the rabbits dusted with a mixture of quartz and aluminum could be distinguished from those dusted with quartz alone by the absence of nodules on the cut surface and of enlarged lymphatic glands. There were many dust-containing areas scattered under the pleura and on the cut surface of the lung.

Microscopic findings in quartz-dusted animals.—The striking feature seen in these lungs was the proliferative response associated with the dust present in the alveoli, peribronchial lymphatic aggregations and mediastinal lymphatic glands. This could be followed through the various stages, resulting in the formation of whorled fibrotic nodules. This response varied but little from lobe to lobe in the same lung, and from lung to lung. The bronchial epithelium showed scattered areas of flattening and loss of cilia. The walls of the bronchial tree showed slight lymphocytic infiltration.

Great numbers of dust cells, distended with finely particulate bi-refringent material, were present in the alveolar spaces. In some alveoli only a few scattered single dust cells were seen that presented regular cell outlines and nuclei that stained well. The enclosing alveolar walls showed little or no change. Other alveolar spaces were tightly packed with dust cells, many of which showed giant cell formation and evidence of degeneration. In such areas the associated alveolar walls showed marked thickening. Many alveolar nodules were seen (Figs. 2 and 4). These nodules varied in appearance and occurred singly or in fused groups of two or three. Single nodules varied from 0.1 to 0.8 mm. in diameter. The pre-fibrotic nodules were composed of elongated dust cells without definite arrangement. In others the peripheral cells were more elongated and arranged in a manner to

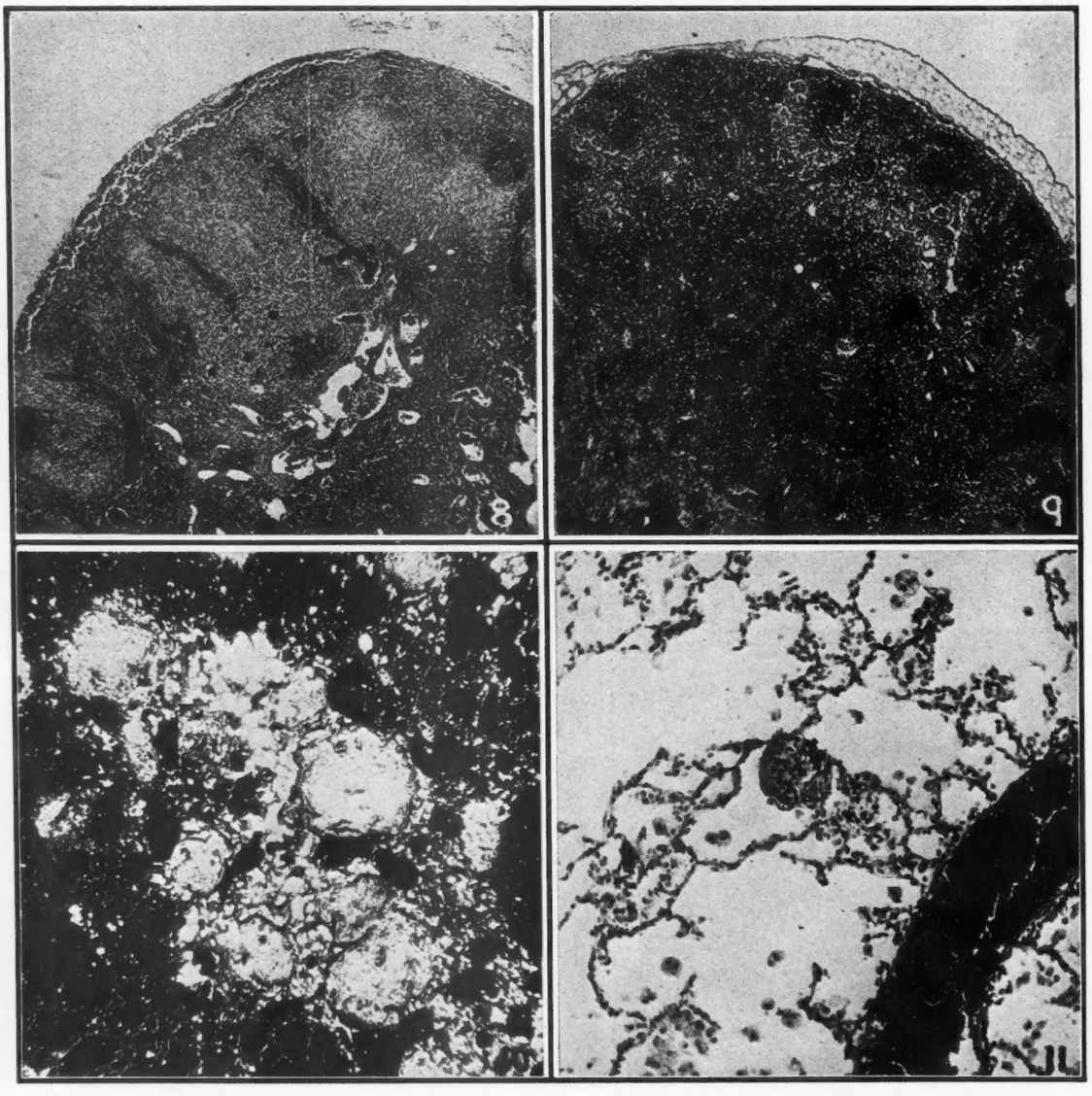

Fig. 8.—Fibrotic areas in a mediastinal lymphatic gland of a rabbit dusted with quartz 16 hours daily for 6 months. **Fig. 9.**—Mediastinal lymphatic gland of a rabbit dusted with quartz and aluminum 16 hours daily for 6 months. Note absence of fibrotic areas, and small number of dust cells present. **Fig. 10.**—Incinerated section of Fig. 2 showing large amount of silicious ash (dark field). **Fig. 11.**—Lung of rabbit dusted with quartz and aluminum 16 hours daily for 6 months, showing slight pre-fibrotic lesion in an alveolus.

enclose a degenerating centre. The fibrous nodules were composed of spindle-shaped cells and reticular fibres arranged in a whorl formation. The peribronchial lymphatic aggregations practically all showed fibrotic areas (Fig. 6) usually arranged in fused whorls, smaller than those seen in the alveoli. In some of the lymphatic aggregations the fibrous reaction occupied about one-half of the total area; others were completely obliterated and enlarged to several times their usual size. All the mediastinal lymphatic glands (Fig. 8) showed varying degrees of reaction, from mere collections of dust cells to well-developed fibrotic areas, formed by the fusion of adjacent nodules. These areas were usually present in the periphery of the gland.

The incinerated sections (Fig. 10) revealed a large amount of silicious ash composed of translucent bi-refringent particles. Practically all these particles were under two microns in their greatest diameter, though occasional ones measuring 5 microns were present. The distribution of the silicious ash corresponded to the distribution of the dust cells and fibrous tissue seen in the stained sections.

Microscopic findings in quartz and aluminum-dusted animals.—The tissue reaction associated with the dust in the lungs of these rabbits was essentially a foreign body response, contrasting in a striking manner with the proliferative fibrotic response seen in the lungs of the quartz-dusted animals.

Great numbers of dust cells were present in the alveolar spaces. Areas comprised of a number of adjacent alveolar spaces, practically filled with dust cells (Fig. 3), were distributed uniformly throughout the lung. Most of the dust cells were contained in such areas, but a few were present in the adjoining alveoli. These cells were engorged with finely particulate bi-refringent particles. They were regular in outline, not elongated, and their nuclei stained well. The dust cells showed little evidence of degeneration (Fig. 5), and much less tendency to giant-cell formation than the dust cells in the lungs of the animals exposed to quartz alone. The walls of the alveoli containing only occasional dust cells were not thickened, and even in those alveoli filled with dust cells only slight thickening of the walls was present.

Few dust cells were present in the peribronchial lymphatic aggregations (Fig. 7) or mediastinal lymphatic glands (Fig. 9). Those present were in small clusters, and were not elongated or associated with a proliferative reaction.

The above description obtains for all the animals dusted with quartz and aluminum, except rabbits No. 93 and No. 96. Besides the above findings the lungs of these animals contained occasional small areas of proliferation in the alveoli and peribronchial lymphatic aggregations. The alveolar lesions were limited to a single alveolus (Fig. 11), and were composed of elongated dust cells without definite arrangement. The areas in the peribronchial lymphatic aggregations were not so large, but had much the same appearance as those seen in the alveoli.

The ash present in the acid-treated incinerated sections of the quartz and aluminum dusted animals was bi-refringent, and the individual particles were of the same size and appearance as those seen in the lungs of the animals dusted with quartz alone. The arrangement of this silicious ash had the distribution of the dust cells seen in the corresponding stained sections.

The liver, spleen and kidneys of the animals of both groups were normal.

DISCUSSION

Chemical.—From the findings as shown in Tables II, III and IV it would seem that other investigators have apparently overlooked the importance of the impurities contained in quartz or other silicious material as being a causative factor in the production of silicosis. It has been found that the alkaline earth carbonates, or carbonates in chemical combination with metals that may be easily decomposed, are responsible for the increased solubility of silicious material. It is also known that the solubility of silica is increased by the presence of small amounts of the carbonates and hydroxides of Mg, Na, K and Ca. Calcium hydroxide and cement, when used in large proportions, as shown in Tables IIIc and IIId, reduce the solubility of silica, but this reaction depends entirely upon the pH of the solution, as shown by Cummings and Miller.[8]

Many compounds of aluminum were investigated and found to be less satisfactory than the metal, since, being unstable, they gave erratic results (Table VII). It took larger quantities to produce the same effect and in some cases, as shown in the literature, certain compounds proved toxic to animals.

Haynes[9] (1931) demonstrated that aluminum hydroxide when inhaled alone caused damaging effects to the lungs of animals, but when mixed with precipitated silica in proportions to produce an artificial shale (80 per cent precipitated silica and 20 per cent aluminum hydroxide) it had a modifying effect on the reaction.

Metallic aluminum (specific gravity 2.68), having a specific gravity about the same as quartz (specific gravity 2.66), will naturally remain in suspension in a dusty atmosphere as long as the silicious particles. We are of the opinion that the aluminum reacts as in the beaker when taken into the lung with the dangerous dusts. That is, that the rapid initial rise and concentration of the solution of the silicious material is inhibited, thereby preventing degeneration of the dust cells and the production of fibrous tissue.

Due to the remarkable results obtained in the quartz and aluminum treated rabbits in conjunction with the beaker results, it seems reasonable to assume that metallic aluminum in small quantities administered in a similar manner will prevent other forms of pneumoconiosis, such as asbestosis, etc.

Comparative solubility tests, run under uniform conditions on silicious materials may indicate the relative fibrosis-producing properties of such materials. The literature does not report any record of damage to the body when small amounts of metallic aluminum are inhaled or ingested. This may be explained by its slow rate of dissolution in body tissues. At the present time we are not in a position to state the manner in which metallic aluminum reduces the solubility of silicious material. There are several ways in which this reaction may be accounted for and work is now in progress along these lines.

Dusting.—We believe that the rapid production of silicosis in the control animals (5 to 6 months) is due to our method of producing an extremely fine freshly fractured dust, uncontaminated with foreign material. The dust counts were kept at a concentration comparable to that produced under blasting conditions in the mine. It is imperative that the use of aluminum for the prevention of silicosis should in no way interfere with the standard practice of ventilation, as large quantities of even inert dust will damage the lung structure.*

Pathological.—The outstanding pathological finding seen in the lungs of the two groups of experimental animals was the marked difference in tissue reaction produced by the dust. The group dusted with quartz alone showed a proliferative fibrotic response, resulting in acute silicosis. Those dusted with quartz and aluminum showed a foreign body response. The slight lesions seen in the lungs of two of the latter group are insignificant when compared with the lesions of the control group. This difference in tissue response cannot be explained by the duration of dust exposure or the amount or the particle-size of the dust present, as the lungs of the aluminum-treated animals contained more quartz of the same degree of fineness, by chemical and microscopic investigation, than those of the control group. It is of interest to compare the appearance of the pulmonary dust cells in the two groups. The dust cells in the control group showed the degeneration, giant cell formation, and elongation to become fixed tissue cells, as well as the migration into the pulmonary lymphatics, which are so typical of the reaction produced by quartz dust in the lung. The dust cells in the lungs of the aluminum-treated rabbits showed little degeneration, much less tendency to giant cell formation and lymphatic migration, and practically no elongation. This is the type of reaction seen when relatively innocuous dusts are present in the lung. In our opinion this difference in tissue reaction is due to the presence of aluminum in the quartz dust inhibiting the formation of a toxic concentration of hydrated or dissolved quartz.

From this group of experimental animals it is impossible to say whether the aluminum is acting locally or systemically, or for what period after the cessation of dusting it will continue to act. These and many other questions will doubtless become clearer when the experiments being conducted at the present time are completed.

CONCLUSIONS

1. It has been shown that the addition of small quantities of metallic aluminum dust almost completely inhibits the solubility of silicious material in the beaker.

2. Seven rabbits dusted with quartz to which less than 1 per cent of metallic aluminum dust had been added showed practically no fibrosis, while 6 control rabbits, dusted with quartz only, showed well developed silicosis.

3. There is a great difference in the solubility of various types of silicious materials.

4. The solubility of quartz is increased by the presence of small amounts of the carbonates and hydroxides of magnesium, sodium, potassium and calcium.

5. The solubility of quartz is reduced by large amounts of calcium hydroxide, but is entirely dependent on the strongly alkaline reaction.

In conclusion, it affords us pleasure to record that the experimental work above described was made possible by the enthusiasm of Mr. R. J. Ennis, General Manager of McIntyre Porcupine Mines, Limited, and by the financial support of the same company, supplied on the recommendation of its President, Mr. J. P. Bickell.

We would particularily express our appreciation of the assistance so generously proferred and supplied by and through the good offices of Sir Frederick Banting and Dr. W. R. Franks, of the Banting Institute, and finally we would record that same appreciation of the splendid work and dependable results provided through the efforts of Mr. F. Bremner, Chief Chemist of the McIntyre Porcupine Mines, Limited, and Mr. H. L. Collins, of the Department of Medical Research.

* Further animal experimentation has been under way for some months, both at the McIntyre Mine and the Department of Medical Research, Banting Institute, the latter using large groups of rabbits, guinea pigs, cats and dogs. Our next paper will be published within the course of the next twelve months.

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TWO CASES OF HYPERPARATHYROIDISM

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PARATHYROID adenoma causing osteitis fibrosa cystica is still sufficiently rare to justify a report of each case. Although many cases have been reported since Mandl's classical case of 1925 it would appear that there is still much to be learned about this condition.

The increased interest in calcium metabolism that has been aroused during the past few years is due chiefly, no doubt, to the great enthusiasm with which the profession took up the subject of hyperparathyroidism. Interest has also been renewed in the pathology of bone, inasmuch as the skeleton in this disease is the seat of great pathological changes.

The following report is about two young women whom I first saw in the well-advanced stage of the disease, and in each case a diagnosis of hyperparathyroidism with extensive bone decalcification was made. Following the removal of a parathyroid adenoma in each patient, the deposition of calcium is followed radiographically in the one case for eighteen months, and in the other for three years. Both these young women were bedridden, profoundly emaciated, with marked osseous deformities, while today they are quite well and carrying on a normal life.

CASE 1

E.D., a female, aged 22, referred by Dr. A. C. Scott.

She had the following complaints: completely bedridden for six months; profound loss of strength (her weight down from 122 to 85 pounds); severe soreness in the limbs, pelvis and chest (any movement caused severe pain); periodic attacks of gastric upsets, with vomiting and dizziness; polyuria and polydipsia.

This patient first consulted a physician on July 10, 1929, complaining of physical weakness, soreness in the limbs and pelvis. This condition persisted, and in December, 1930, she developed a swelling in the right mandible. She consulted a dentist who said it came from a tooth and opened into it through her mouth, but said blood alone escaped. January, 1931, another dentist took a radiograph, and said she had osteomyelitis and curetted the cavity. In September, 1931, a tooth close to the swelling was extracted and the cavity again curetted. She gradually became weaker and in November, 1932, became bedridden. After five months' complete confinement to bed the "sides of her chest fell in" (patient's statement). Her physician was called and a radiograph taken of her chest showed almost complete destruction of her ribs. At this time I was consulted by telephone and suggested a complete radiographic study of the skeleton and estimation of the blood serum calcium. The latter was 18 mg. per 100 c.c. of blood, and radiographs showed extensive decalcification of many bones. I went to see this patient in a cottage hospital in a town in a neighbouring province.

Examination revealed a frail, emaciated young woman, unable to move her legs or feet because of pain. There was a marked deformity of the chest, the sides of which expanded and retracted with respiration. There appeared to be separation of the costochondral junction of the second to sixth ribs on the right side and of the third to sixth ribs on the left side, the costal cartilages sticking out like fingers, their ends covered only by skin, the anterior ends of the ribs having fallen backwards. This made respiration rather difficult. Pulse 100, blood pressure 100/66.

After viewing the radiograph and the serum calcium having been checked by a reliable laboratory (18 mg. per 100 c.c.), a diagnosis of hyperparathyroidism was made. The emaciated condition of the patient made examination of the neck easy. There was a suggestion of a palpable irregularity low on the right side against the vertebral column, but this was rather indefinite.

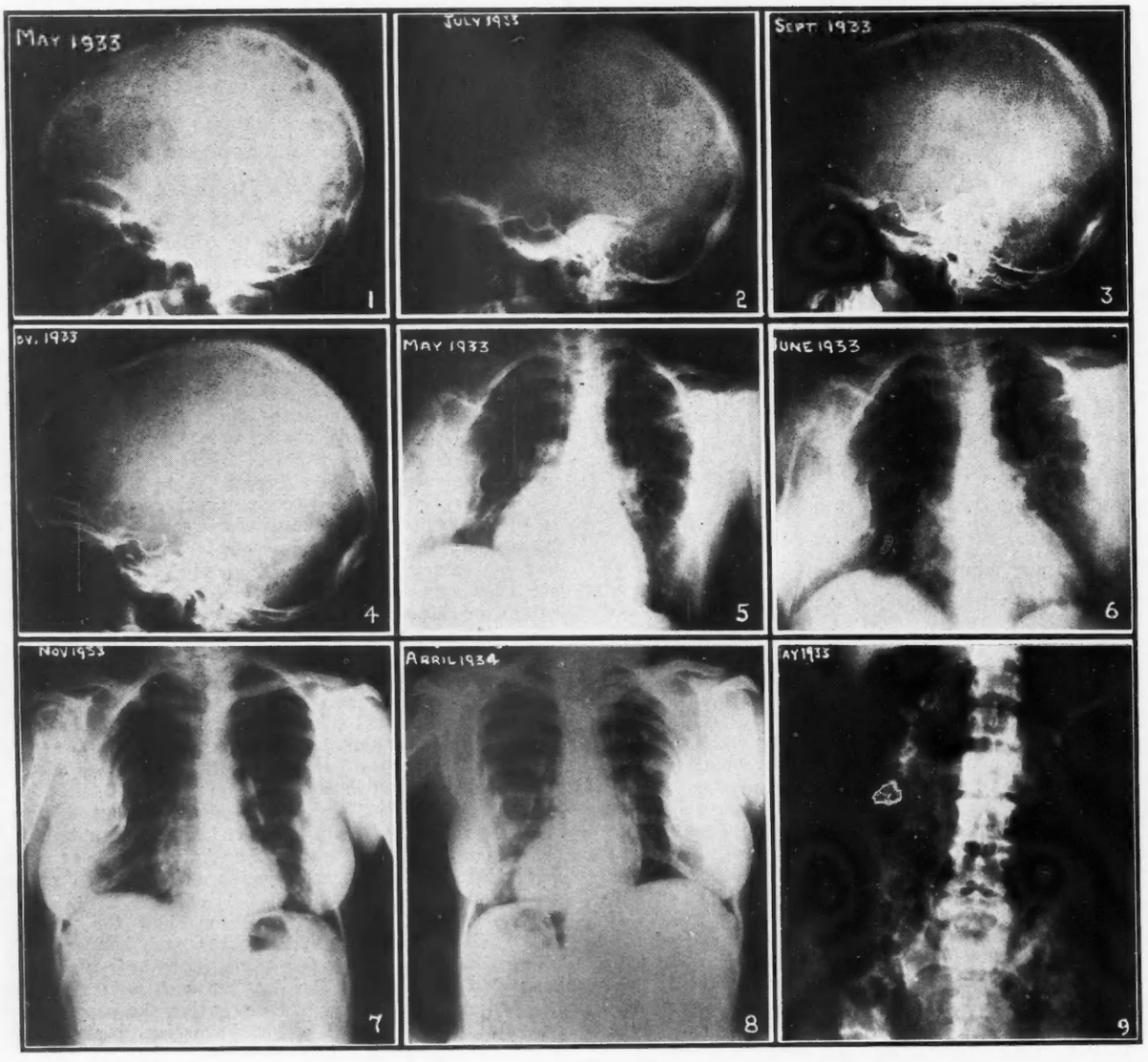
General inhalation anæsthesia seemed inadvisable because of the poor general condition of the patient and the partially collapsed bony cage of the thorax, so the neck was explored under local anæsthesia (novocaine) on May 1, 1933. What appeared to be three normal parathyroid bodies were demonstrated, the two lower and the right upper. The left upper was not seen and there was no sign of a tumour. The mediastinum was then explored, and I felt a globular irregularity against the vertebral column just below the level of the right sterno-clavicular joint. This small mass was exposed and found to have a smooth glistening capsule. It was elevated, two arteries were clamped, and the small tumour, which was spherical and about 2.5 cm. in diameter, was easily delivered. Photographs and photomicrographs of this adenomatous tumour, are shown below, with the radiographs and the blood serum calcium record.

An attempt has been made to show the rate at which calcium is redeposited so that each bony part is featured with its consecutive radiographs before another bony part is shown. The date of each radiograph is stamped on the picture. The negative shadows in the frontal area in Figs. 1 and 2 have been replaced by positive shadows in Figs. 3 and 4, showing that a greater amount of calcium than normal has been laid

down, in at least this localized area, suggesting calcification of the diploe between the outer and inner tables of the skull. Fig. 5 shows very little calcium in the ribs, while Figs. 6, 7, and 8 show the gradual deposition of calcium with the marked deformity of the ribs as stated earlier in the text. The patient has regained bony stability of the thoracic cage, but with some persisting deformity. Figs. 9 and 10, taken 16 months apart, show the profound contrast in the calcium content of the iliac bones and the persistence of the calcium shadows in the right kidney, with little, if any, diminution in intensity. Figs. 11, 12 and 13 show the upper ends of the femurs to have been completely recalcified in six months. No further advance seems to have been made in Fig. 14, five months later. Note the great decrease of the angle at the neck and shaft of each bone, requiring osteotomy to correct this deformity in the left femur, sixteen months after the parathyroidectomy.

The marked coxa vara can readily be understood when one sees the almost complete absence of calcium in the upper end of the femur. Part of this deformity, no doubt, was brought about by weight-bearing before she went to bed, but in the later stages of the disease in this patient, it is quite conceivable that the muscles of the hip and thigh might easily produce sufficient pull to lessen the angle at the neck and shaft. In this case I think some extension should have been applied before calcium was redeposited, in the hope of lessening the deformity. When I saw this patient again in September, 1934, sixteen months after operation, she had a mild "scissors leg" gait, due chiefly to the marked diminution in the angle at the neck and shaft of the left femur causing marked adduction of the shaft. An osteotomy of the upper end of the shaft was carried out to correct this deformity, and the patient obtained quite a good result, walking quite well.

The "moth eaten" character of the bones seen in Fig. 15 has disappeared in Fig. 16.



Case 1

TABLE I.

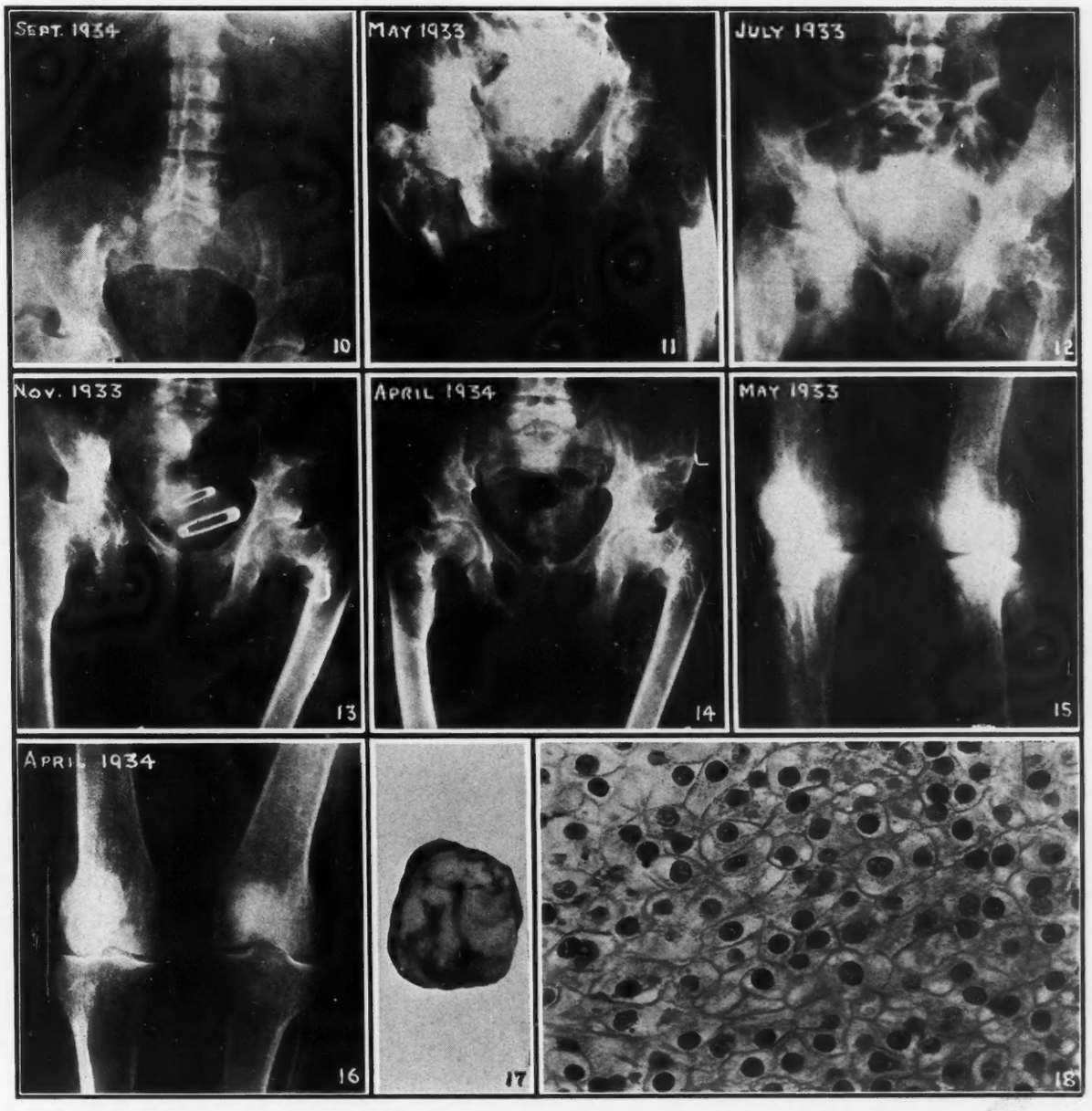
BLOOD CALCIUM RECORD OF E.D. DONE BY QU'APPELLE SANATORIUM STAFF. (BEFORE OPERATION, MAY 1, 1933, BLOOD CALCIUM WAS 18-19 MG. PER 100 C.C.).

May 1933	*Mg. per 100 c.c.*	*May 1933*	*Mg. per 100 c.c.*
2	14	13	7.6
3	10	15	7.3
4	9	17	7
5	9	19	6
6	8	21	8
8	8.1	24	8.6
9	7.9	27	9.6
10	7.7	30	9.7
		June	
11	7.6	3	10.4

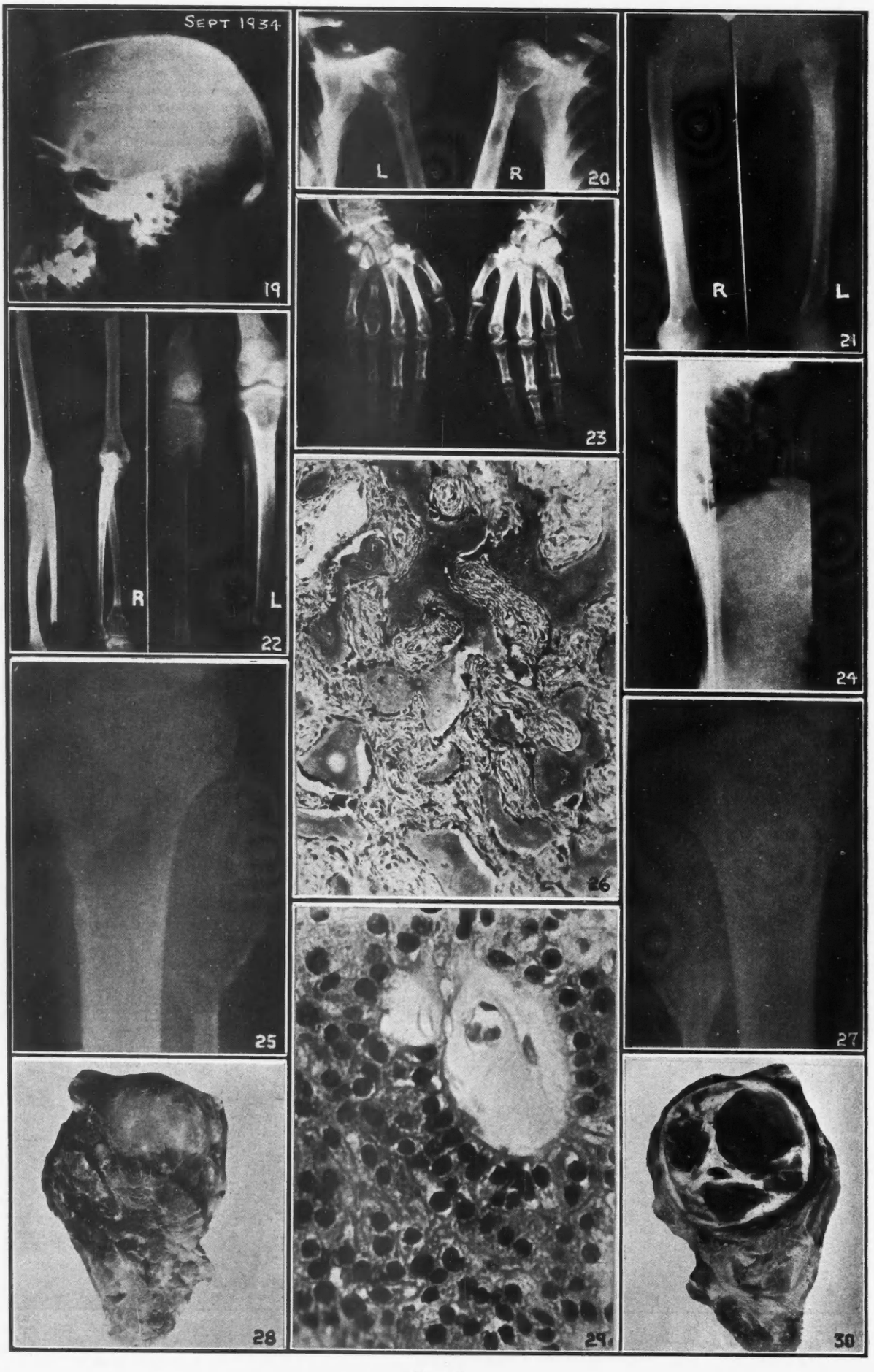
Note the sudden drop in calcium following parathyroidectomy, and its persistence. No clinical manifestations of tetany were noted.

Report on specimen removed at operation from E.D., May 1, 1933, by Dr. Fahrni.—"The tumour is spherical, the size of a large cherry (2.5 cm. in diameter) and weighs 3.88 g. It is perfectly encapsulated (see Fig. 17). The cut surface is an opaque white and is divided into three areas sharply separated from one another. Microscopically the specimen presents a typical picture of parathyroid tissue. The arrangement of the cells is perfectly regular, and the size and shape of the cell body and nucleus of each cell are also uniform. The condition, therefore, may be regarded as an adenoma or a hyperplasia of the parathyroid." (See Fig. 18).

One interesting feature of this case was the unusual situation of the parathyroid adenoma. In cases reported elsewhere this has been the reason why the tumour was missed at the first and sometimes at the second operation. The tumour of the mandible for which the patient had been operated on by dentists on three occa-



Case 1



Case 2

sions was no doubt part of the general disease.

The radiographs showing calcium calculi in the right kidney before operation, with no apparent diminution sixteen months later, suggest that there is little probability of these calculi disappearing. In this case there was never at any time any evidence of disturbed kidney function, the urine at all times being found apparently normal on full examination, and her renal function was normal.

October 10, 1934, this young woman had normal strength and weight, walked quite well, and she stated she led quite a normal life.

CASE 2

A female, aged 17, referred by Dr. H. P. H. Galloway.

This girl had noticed some general weakness and only slight soreness in her legs for a month before she stumbled and fell in May, 1934, and was unable to get up. She was taken to the local hospital where she was treated for a fracture of the upper end of the left tibia. She remained in hospital for fifty-four days. She was sent home, but was unable to walk and was quite weak and had lost 24 pounds. She had no polyuria, nor did she consume an abnormal amount of fluids.

She was the eldest of five children, the others being quite healthy. She menstruated at 16, but only every two months since. Dr. Galloway was called to see her on September 29, 1934, and brought her to Winnipeg, where I saw her in consultation with him.

Examination revealed a small, rather poorly nourished girl, somewhat infantile in appearance. Her weight was only 65 pounds; skin dry and sallow; pulse 120; blood pressure 140/88; and temperature 100° F. The thyroid appeared normal, but beside the left lower pole I could see and easily palpate a globular mass the size of a small walnut. There was obviously an ununited fracture of the upper end of the left tibia with 2¼ inches of shortening of the leg below the knee, swelling of the upper end of the right fibula, swelling of the lower end of the right radius, and a firm swelling in the middle of the right mandible. A well-marked lower dorsal kyphosis was also present. Radiographic study of the skeleton showed extensive decalcification, with apparent expansion of the bone in several sites, as shown by some of the radiographs below.

Blood serum calcium 15.4 mg. per 100 c.c.; blood serum phosphorus 2.3 mg. per 100 c.c.; red blood cells 3,940,000; hgb. 60 per cent; colour index 0.76; red blood cells normal except for mild anisocytosis; white cells 11,900; normal differential count.

Diagnosis.—Parathyroid adenoma.

October 3, 1934, operation under local anæsthesia (novocaine) revealed a globular tumour, about one inch in diameter, lying just lateral to the lower pole of the left lobe of the thyroid gland and attached loosely to its capsule. This growth was easily removed.

Some of the radiographs of the bones are shown, and the photographs and photomicrograph of the adenoma.

I wish to call attention to the multiple giant-celled, localized expansions of bone (osteoclastomas) in this case, in contrast to their absence in Case 1. These are well shown in Fig. 22 (upper end of the left tibia at the site of fracture, and upper end of right fibula and lower end of right radius) and in Fig. 23 (4th right metacarpal bone). In Fig. 24 the partial collapse of the bodies of two vertebræ is shown, and this is the cause of the kyphosis mentioned in the text. Fig. 25 (right leg) was taken on September 30, 1934, four days before the parathyroidectomy, and Fig. 27, November 8, 1934, six weeks later, shows the rapidity of recalcification of both the defect in the upper end of right tibia and the greatly expanded and decalcified upper end of the right fibula. Fig. 26 is a photomicrograph of a biopsy specimen taken from the centre of the expanded upper end (osteoclastoma) of the right fibula on November 8, 1934, the same date as Fig. 27. It shows the active reformation of calcified bone although this process seems little more than half completed. The pathologist's report relating to Fig. 26 is as follows.

"*Bone biopsy: microscopic.* — The compact bony covering is very thin, and the cancellous portion shows marked osteoporosis with many osteoclasts lying adjacent to bone cancellæ. The chief change is a fibrous metaplasia of the bone."

TABLE II.

BLOOD SERUM CALCIUM AND PHOSPHORUS FINDINGS

1934	*Serum calcium*	*Serum phosphorus*
Sept. 30	15.4	2.3
Oct. 1	15.4	2.3
" 3	operation	
" 5	8.6	2.5
" 6	8.6	2.8
" 7	7.5	–
" 9	7.8	2.4
" 10	7.5	–
" 11	7.0	–
" 12	6.7	2.3
" 13	6.3	–

Note the sudden drop in calcium following parathyroidectomy and its persistence. No clinical manifestations of tetany were noted.

Pathologist's report. — "Specimen consists of a round encapsulated mass, 3 cm. in diameter and weighing 13.5 g. A small amount of thyroid tissue is adherent to the external surface (Fig. 28). The cut surface is cystic (Fig. 30) with areas of pinkish-yellow, solid tissue running through the cysts filled with gelatinous material. Microscopically the specimen consists of sheets of cells similar in appearance to those of parathyroid and showing an indefinite alveolar arrangement. A marked feature of the cystoplasm is granularity, which in some places has gone on to vacuolization. There are large and small collections of colloid material, some of which stains intensely with eosin and some faintly. This material is evidently rich in cholesterol, as evidenced by large numbers of lipoid-filled phagocytes. This is a parathyroid adenoma." (See Fig. 29).

The patient left the hospital for her home in a neighbouring town three months after operation. She was walking quite well except for the shortening in her left leg for which a "built-

up'' boot was to be made. There was also some dorsal kyphosis, which suggested that a greater degree of extension of the spinal column at this level should have been maintained during the early post-operative weeks. Recalcification of the skeleton seemed to have been fairly well completed, and the swellings at the site of the osteoclastomas had become much smaller. Her secondary anæmia was much improved.

On March 2, 1935, the patient came in for examination and appeared quite well and active.

In conclusion I wish to thank Dr. Scott who took all the post-operative responsibility in Case 1, as I left for home the day of the operation and did not see the patient again until thirteen months later. It was he who took the radiographs and who supervised her convalescence. Dr. Wherrett, then of Qu'Appelle Sanatorium, did the blood calcium estimations, for which I wish to thank him, and also I wish to thank Dr. A. P. McKinnon who was associated with me when the osteotomy of the left femur was done, and Dr. H. P. H. Galloway who invited me to see patient 2 in consultation with him, and later referred her to me for treatment, also Dr. Wm. Boyd who reported on the parathyroid tissue removed in each case.

MINUTE OXYPHIL ADENOMA OF THE PARATHYROID ASSOCIATED WITH CALCIUM DEPOSITS IN THE KIDNEY*

BY BRUCE CHOWN, M.D.

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THE following case is reported because of the association of a minute oxyphil adenoma of the parathyroid with small calcium deposits in the kidney, and may be considered a continuation of previous observations[1] on the effect of mineral excretion upon the kidney. The full report of the clinical course and mode of death will be made by Dr. F. A. Benner, through whose kindness I have been able to study the particular aspect of the case here considered.

CASE REPORT

Mrs. Nellie C., aged 46, died in Grace Hospital April 21, 1936, from rupture of an aneurysm of the circle of Willis, having been ill in all 17 days. In 1927-28 she had suffered from left lumbar pain and headache, lasting on each occasion a few days. In June, 1928, a left nephrectomy was performed for nephrolithiasis. Following the operation the urine, which had been loaded with pus, cleared up save for a trace of albumin. Periodic headache continued, and in August, 1929, a subtotal hysterectomy was done. The patient's subsequent history is not known until the onset of her final illness. During this illness the urine (3 examinations) had a specific gravity of 1.002, 1.005 and 1.020; no albumin; no sugar sediment, none on one examination, a few granular casts, red and white cells on a second, and 5 to 10 pus cells per high power field on a third. The blood urea nitrogen was 24 to 28 mgm. per 100 c.c. Blood pressure was 232 to 130 systolic and 160 to 90 diastolic, being affected by lumbar punctures and venesections. The blood Wassermann reaction was negative.

Autopsy was performed at the undertaker's 15 hours after death, the body having been embalmed. The body was that of a well nourished white woman appearing younger than her given age of 46; breast development good; skin colour fair, without abnormal pigmentation. There was a pea-sized aneurysm of the right communicating branch of the circle of Willis, which had ruptured, causing extensive hæmorrhage at the base, large clots in the posterior fossa and a thin film of blood over the vertex. The pituitary and pituitary fossa were not enlarged but there was much blood about them. The thyroid was of average size. There was a single hard adenoma 1 cm. in diameter in the right lobe. The four parathyroids were dissected out. They were pale brown in colour, flat, long ovoids, about the size and shape of a cucumber seed. The longest was 8 x 4 x 2 mm. The thymus was not enlarged but unfortunately it was mislaid at the autopsy. Heart, lungs, liver and spleen were not remarkable. The left kidney was absent. The right was somewhat enlarged, pale (? embalming fluid), with a few scars on the surface at which points the capsule was adherent. On section it felt a little gritty to the knife. The cortex was broad and fairly sharply defined. The pelvis and ureter appeared normal. No stones were present. The adrenals were of average size, the cortex brownish yellow, and the medulla white. The uterine cervix was present as a small stump. The ovaries were of good size, approximately 35 x 17 x 8 mm., and contained both follicles and luteal remnants. The skull was thick and rather dense. The vertebral bodies cut fairly readily with a chisel.

Microscopically, in the *pituitary* there was vascular engorgement and a few minute hæmorrhages. The cells of the anterior pituitary had the average irregular distribution of types. There were a number of small colloid-filled acini in the region of the pars intermedia and still smaller ones for a short distance into the pars anterior. The pars posterior appeared normal. Three of the *parathyroids* were entirely normal, with an average distribution of chief and normal oxyphil cells. In the fourth was an adenoma (Fig. 1), measuring in section 2.2 x 1.0 mm., made up of anastomosing cords of oxyphil cells. These (Fig. 2) varied in size from that of a chief cell (about 6 to 8 micra) to five or six times this size. The smaller cells tended to have a scant cytoplasm, the large ones a solid one as in the normal oxyphils but varying in staining intensity from cell to cell. The nuclei of the small cells were correspondingly small (about 5 micra), those of the large cells reached a size of 15 micra. They had a sharp nuclear membrane, a fine chromatin network and prominent nucleoli. The picture suggested functional activity. In the *thyroid* there was great variation in the size of the follicles, abundant colloid, small interstitial lymphocytic collections. There was some tendency to adenoma formation but no epithelial hyperplasia. The *ovary* and *adrenal* were not abnormal.

* From the wards of Grace Hospital and the St. Agnes Guild Laboratories of the Children's Hospital of Winnipeg.

In the *kidney* were minute deposits of calcium, almost entirely confined to the outer 0.5 cm., of the cortex in the tissue examined. They were quite inconspicuous, yet numbered as many as 120 to the square centimetre. Each deposit was made up of a group of granules 2 to 8 micra in diameter, the whole deposit tending to be round, about 30 to 40 micra in diameter. Thirty deposits were closely examined. One was apparently intratubular and associated with pink homogeneous material. One was deposited on a plaque of epithelial cells. The remaining 28 were interstitial. They were associated sometimes with a blue material that did not stain black with silver nitrate, sometimes with a few inflammatory cells, a little pink homogeneous substance or slight fibrosis. They lay close to tubules, two very definitely distorting the neighbouring tubule. Frequently a minute blood vessel lay beside the mass. The kidney parenchyma was diseased. An average square centimetre of cortex contained 30 glomerular pearls and 135 other glomeruli. Most (26 out of 30) of the completely destroyed glomeruli were in the outer 2 mm. of the cortex, and tended to occur in groups of 2 to 4. Of the other glomeruli some were entirely normal, some congested, in some the basement membrane of the capsule was thickened or there was pericapsular fibrosis. There were still slighter changes in the tubules; minute dilatations with epithelial flattening, a little albumin, an occasional leucocyte, a rare pressure deformity from a calcium deposit. There were small foci of interstitial fibrosis in the outer part of the cortex.

In the bone (9th thoracic vertebra) there was no fibrosis or thickening of the endosteum. It appeared entirely normal.

DISCUSSION

The case history is unhappily fragmentary, yet there are three facts which are definite and appear important; first that the patient had kidney stone eight years ago, second, that at time of death she had calcium deposits in the remaining kidney, and third, that there was present a minute oxyphil parathyroid adenoma with histological appearances suggesting physiological overactivity. In addition the kidney was mildly pathological, the picture suggesting an early nephrosclerosis, yet not being quite typical.

Turning first to the adenoma, Castleman and Mallory[2] in their careful study of the parathyroid glands in 25 cases of hyperparathyroid-

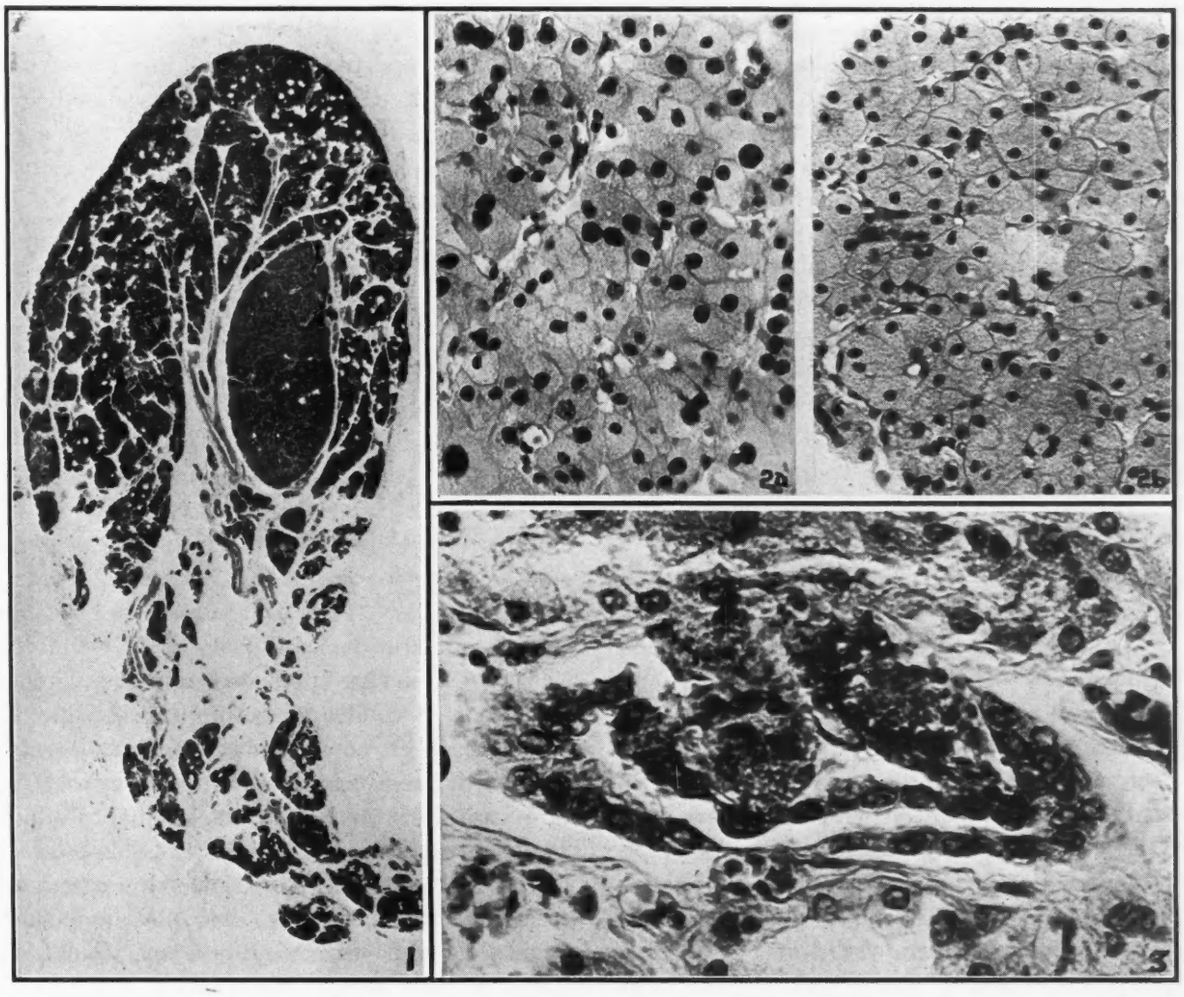

Fig. 1.—Section of parathyroid with contained adenoma. Scale equals 1 mm. **Fig. 2.**—The adenoma (a, left) compared with a normal island of oxyphils from the same gland (b, right). x 300. **Fig. 3.**—Extra-tubular calcium mass distorting a tubule. x 550.

ism and in 150 routine autopsies came to the conclusions that the oxyphil cell was probably an inactive, involution product. They were doubtful of the cases reported as oxyphil adenomas. Sections from the present case were submitted to Dr. Castleman, who kindly allows me to quote his opinion. "The oxyphil cells in the tumour are enlarged, and their nuclei are very much larger than the nucleus of a normal oxyphil cell. It is certainly not an island of oxyphils, such as that normally found in elderly individuals. I would call it a true adenoma."

Castleman and Mallory had found no parathyroid adenomas in their 150 routine autopsies. On the other hand Pappenheimer and Wilens,[3] in their study of the parathyroids in kidney disease, reported finding small oxyphil adenomas in 3 of 27 autopsies on nephritics and in 2 of 72 autopsies on non-nephritics. These figures suggest that the present adenoma was a normal anatomical variant. Dr. Pappenheimer was good enough to send sections of these and other pathological parathyroids for comparison with the one here described. In none of his did the histology correspond with this one. It is my opinion that this is a true functioning adenoma.

The next point that arises is whether this adenoma produced the calcium deposits in the kidney. In the absence of all chemical evidence in this case we can only make the general statements that parathyroid overactivity does cause calcium to be deposited in the kidney, that it is then deposited in the paratubular interstitial tissue and that it was so deposited here. The picture in the kidney suggests, but does not prove, a mild degree of hyperparathyroidism. On the other hand the one bone examined (9th thoracic vertebra) shows no histological evidence of hyperparathyroidism. This however does not disprove the presence of some degree of parathyroid overfunction since we[1] have repeatedly observed in our older rats that parathyroid extract injections may result in calcium deposition in the kidneys without discernible histological evidence of bone resorption.

As to the possible relationship between the present adenoma, the present calcium deposits, the earlier kidney stone and the hysterectomy one can only make fruitless guesses. And one is left to wonder whether long continued mild mineral assaults produced the nephrosclerosis that was present.

SUMMARY

A case is reported in which a minute oxyphil adenoma of a parathyroid was associated with small calcium deposits in the kidney and early nephrosclerosis in a woman who had previously suffered from kidney stone.

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PREVENTION OF POISON IVY DERMATITIS BY THE INTRAMUSCULAR INJECTION OF "RHOLIGEN" (RHUS TOX. OLEO-ANTIGEN)

BY A. H. W. CAULFEILD, M.B., F.R.C.P.(C.)

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THIS report on the prevention of dermatitis due to poison ivy is the direct result of the investigation and treatment of dermatitis due to contact with tulip bulbs and ragweed.[1] Different observations made with those few cases led me to believe further work with the ether-soluble fraction of plants holding comparable toxic properties was definitely indicated. In the first place the therapeutic result of a most satisfactory prevention by a series of intramuscular injections was most striking with the case of tulip-bulb dermatitis, and it is to be noted that the prevention has persisted without further treatment. Secondly, I was impressed with the wide range in potency of different extracts made with what appeared to be relatively insignificant variations in the technique. Following the preventive inoculations the character of the patch test showed marked alteration—an alteration which viewed from one angle suggested the skin sensitization had been abolished.

The relative paucity of persons contracting a dermatitis from either tulip bulbs or ragweed constituted a definite handicap, and led to

the thought that poison ivy (*Rhus toxicodendron*) might prove a suitable substitute from which to prepare extracts with a technique comparable to that found most successful with tulip bulbs. This extract can conveniently be labelled "Rhus tox. oleo-antigen". Essentially, it is the ether-soluble fraction of the poison ivy plant taken up in sterile mazola (corn) oil. For the purpose of brevity I have coined the word "Rholigen".

I. CONTROLS

Two types of control were made in addition to the usual sterility tests. The first consisted of the intramuscular injection of 1 c.c. of the stock oleo-antigen into rabbits and guinea pigs. This resulted in no visible or palpable reaction, either immediate or delayed, and the animals gave no evidence of any irritation.

The second type of control with the "normal" human being was carried out only after the results of patch testing in the case (F.G.M.) described below were known. Amongst a group of normal people already tested for suitability for the Prausnitz-Kustner test H.D.R. gave the following history.

He had been brought up on a farm and had weeded out poison ivy without any resulting dermatitis or irritation. He was patch-tested with the oleo-antigen, first in the 1/100 dilution and then in the 1/0 dilution or stock solution. Both tests were negative. A short series of intramuscular injections were given, beginning with the 1/1,000 dilution and ending with the 1/25 dilution. No appreciable reaction or discomfort resulted from any of the injections, and following the series he remained patch-test negative to the undiluted oleo-antigen.

This seems to support the theory[2] I had evolved in the investigation of dermatitis due to tulip bulbs, and, also with poison ivy dermatitis, namely, that the cause was a lack of normal antibody-like substance and was totally dissimilar to the underlying factors in the typically human instance of allergy, namely, hay-fever, in which the cause is most probably the presence of an abnormal antibody.

The serial dilutions cited in this paper from 1/0 to 1/10,000 were based on dilutions of the undiluted 1/0 or stock solution with sterile mazola oil and not estimated from the original weight of the plant used for extraction. Microscopically, the undiluted material showed numbers of flocculent masses. These showed sparsely as fine flocculi in the 1/10 dilution and were absent in the 1/25 dilution.

II. SPECIFICITY AND POTENCY

At first the undiluted Rhus tox. oleo-antigen was added to the group of substances to be used for those cases in which patch testing was indicated — especially those suffering from a seasonal (essentially summer) dermatitis. The results were negative in most, and this included a group in which definite etiological agents such as tulip bulbs, ragweed, sheep's wool, etc., gave clear-cut positive results. The technique with oleo-antigens has been described previously,[1] but might be reviewed briefly as follows, as it differs considerably from other reports in which the application is described as painting of the skin surface and in which the duration is continued for from two to three days, or even longer. The rounded tip only of a 2 mm. glass rod is dipped in the oleo-antigen and then pressed lightly to the skin of the forearm. This leaves a thin film of the oily extract, roughly measuring from 1 to 2 mm. in diameter—about the size of the head of an ordinary pin. A wisp of cotton wool is applied to the spot of oil and covered with a piece of cellophane approximately 30 mm. square. The cellophane is held in place by anchoring two of the corners with about half inch lengths of half-inch adhesive tape. This eliminates a "plaster dermatitis" and is very comfortable. A few turns of gauze bandage are finally applied and appropriately held in place by small strips of adhesive. The duration in general has been 24 hours, never more, and in many instances for from 15 to 18 hours. This was the technique employed until after the first case giving a past history of poison-ivy dermatitis was tested. As the results with this case were startling and initiated a change in the technique it will be given in detail.

F.G.M. gave a history of having had two, possibly three, attacks of poison-ivy dermatitis, the last occurring five years ago. Since the last attack there had been summer outings, presumably affording opportunities for further attacks. From the description of the attacks there seemed no reason to assume undue severity.

On August 4, 1936, four patch tests were made, including the Rhus tox. oleo-antigen. Eighteen hours later they were all negative except with the Rhus tox. oleo-antigen.

In the test area there was a definite œdema corresponding precisely to the space covered by the cellophane, and in addition a closely spaced accumulation of fiery red pin-point dots. The site at this stage was not itchy, but in a few hours it became intensely irritating and vesicles began to form. The arm when seen four days after the application was enormously swollen. One large vesicle was present over what seemed to be the site of the original reaction; a

second similar vesicle was present on the upper arm, apparently from contact. There was literally no space on the entire forearm which was not occupied by vesicles of varying sizes. The patient had applied calamine lotion, and the arm when held up simply dripped. Over 5.0 c.c. of vesicular fluid was withdrawn from one of the larger vesicles which almost immediately refilled itself. Patches were apparent on the face and elsewhere. Hospitalization and frequent dressings were necessary and were continued for over four weeks. Months after, irritation and some discoloration of the forearm would appear on exercise such as dancing. The severity of this reaction when seen for the second time on August 8th seemed incredible both to myself and fortunately also to the patient.

III. Quantitative Patch Testing

The extreme severity of the reaction induced in the preceding case (F.G.M.) by using the oleo-antigen in undiluted strength suggested the necessity of using serial dilutions of 1/10, 1/100, and 1/1,000. The dilution of 1/100 has so far been most frequently employed. As the range of positiveness even with this dilution varies extremely the following tentative classification has been adopted in reading the results. Though the degrees of reaction merge one into the other, there are certain definite features which aid the classification.

Negative reaction.—No appreciable change on removal of the patch test and no subsequent dermatitis.

One plus reaction.—In this group two or possibly three divisions seem advisable, such as mild, moderate, and strong. (1) The mild reaction. On removal the skin appears normal, but in 24 to 36 hours a reddened dry dermatitis appears which may last only a few days. It remains dry and the spread is less than the area originally covered by the cellophane. (3) The strong reaction. On removal the skin may appear to show a questionable degree of œdema, but in 12 to 24 hours there is a very distinct area of reddened dermatitis which remains dry, spreads up to or beyond the cellophane area, and lasts up to about four weeks or more. Such a patch is very itchy, and for most some soothing application is necessary. The moderate reactions lie between the mildness of 1 and the relative severity of 3. All in this group should be called delayed; the different degrees depend upon intensity and duration. The exact duration is difficult to express in precise days, because, though maximum intensity is rapidly achieved, disappearance is extremely gradual. In all reactions except the one plus mild, the duration does not vary in proportion to the severity of, for example, the two, three, and four plus reactions. The latter are very intense and distressing, but probably do not last more than twice as long as a one plus severe.

Two plus reaction.—On removal the area covered by the cellophane is definitely œdematous, with possibly one or two punctate areas. Within 24 to 48 hours slight vesiculation occurs and this feature persists for several days.

Three plus reaction.—On removal, the area covered by the cellophane is œdematous and there are many punctate areas. In a few hours vesiculation occurs and spreads to about a 60 X 60 mm. area. The vesiculation lasts for about three weeks, and frequent dressings are necessary.

Four plus reaction.—In this group, also, subdivisions would seem advisable, as presumably a case sufficiently sensitive might be encountered to give as severe a reaction with this dilution as resulted in the individual (F.G.M.) with undiluted oleo-antigen. Reactions in this group show on removal a marked œdema of the area covered by the cellophane, with brilliant red pin points scattered about. The severity of the reaction seemingly is indicated by the density and number of red points present on removal. In a very few hours vesiculation appears, becomes intense, and the entire reaction spreads. The most intense so far encountered with the dilution of 1/100 spread to approximately half the surface of the lower arm, and lasted a long but indefinite period of time. (See Case 4, McC.D.).

IV. Correlation of Quantitative Patch Testing and Severity of Clinical Attacks

Up to the present no person with a past history of having suffered an attack of poison-ivy dermatitis, no matter how slight, has failed to give a positive test with the 1/100 dilution. The following examples will suffice to show this.

A.G.C. regarded himself as immune to poison ivy, but two years ago had a very mild eruption confined to the fingers which followed some weeding out of the plant about his summer residence. A patch test gave a one plus mild reaction lasting only 4 to 5 days. O.M.D. had a slight attack about 30 years ago, but none since, though there had been presumably other exposures. The patch test gave a one plus moderate reaction (see Fig. 1). S.M. had what would seem to have been a relatively mild attack five years ago, and the patch test was one plus severe (see Fig. 2).

The results so far have shown that all who have given a one plus (delayed) reaction have had relatively mild attacks which have not been repeated. It would thus seem that probably more than casual exposure is necessary with this group. Those in whom three and four plus reactions have been obtained have given a history of severe attacks each year they have had their usual summer exposure. For one reason or another it has been impossible to take photographs of the severer reactions (three and four plus).

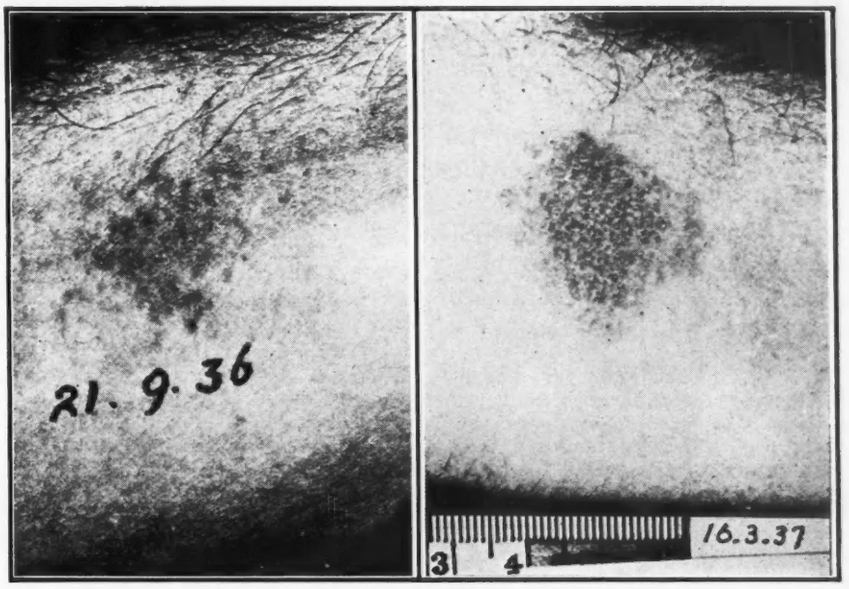

Fig. 1 Fig. 2

Fig. 1.—O.M.D., three days after removal. On October 5th the area was greater but less intense—a one plus moderate reaction. **Fig. 2.**—S.M., seven days after removal. Dressings were continued for 3 weeks and the site was detectable 8 weeks after—a one plus severe reaction.

V. The Character of the Reactions Following Intramuscular Injections

Two types of reaction have so far been encountered. The milder type consists of a local irritation—a deep-seated feeling of itchiness—which appears about three to four hours after the injection, and on an average continues for about four to six hours. In the severer type the local itching continues and there appear somewhere on the skin of the body either definite swellings, brownish in colour, or a patch of dermatitis. If vesiculation results it seemingly appears at once. These remote cutaneous manifestations may be far distant from the site of inoculation, such as on the skin of the thighs, hands, or centre of the chest when the injection was given in the muscles of the shoulder girdle. There have been no systemic sensations and the term "remote" rather than "general" reaction seems more applicable. The first relatively severe remote reaction was encountered in the treatment of a three plus patient when a tenfold increase to the dose of 0.25 c.c. of the 1/1,000 dilution was given. The likelihood of reactions mild or severe would seem to be in inverse proportion to the rapidity of increase, and probably can be almost entirely avoided if so desired by adjusting the increase to minimal amounts and increasing the number of injections.

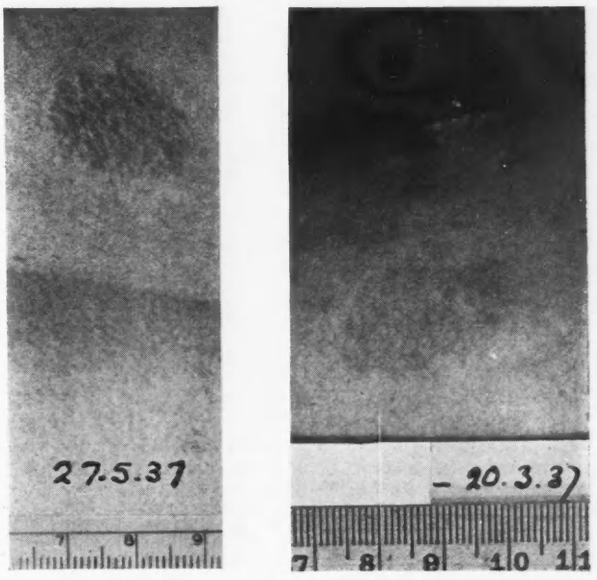

Fig. 3 Fig. 4

Fig. 3.—N.M., following treatment; 4 days after removal slight itching at times only. This is a one plus mild reaction. Patch test before treatment was a two plus. **Fig. 4.**—F.H., following treatment; two days after removal. Slight irritation continued for 2 to 3 days and by the 6th day the area was barely detectable. This is a one plus mild to moderate reaction. The patch test before treatment was a three plus.

VI. Case Reports Illustrating the Results of Treatment

The past histories of the four cases* selected provide, I feel, adequate proof of the effectiveness of preventive treatment. The marked change induced in the quantitative patch test, done before and after treatment, is regarded as a better indication of the degree of protection afforded by treatment than the more or less chance clinical result which might be obtained on re-exposure to the same regional environment. Because of my belief in this interpretation of the tests, publication is made now rather than later on.

Case 1

N.M., female, aged 12. For many summers the same exposure induced attacks of poison-ivy dermatitis. In more recent years her family thought there was a definite tendency towards amelioration, but the girl herself stated that even in the last year or so small irritating patches appeared and persisted in an irregular fashion. An initial patch test (dilution 1/10) on November 19, 1936, gave a *two plus reaction.* Following treatment† the test was one plus mild. (See Fig. 3.)

Case 2

F.H., male, aged 20. His history showed he had suffered yearly attacks of dermatitis ever since he could remember on going to his people's summer resort "The Beaches". The severity varied considerably in degree, and apparently corresponded to some extent with the care he exercised in avoiding direct contact with the poison ivy plant. The involved areas were the forearms, feet, face, and various areas of the trunk. An initial patch test (dilution 1/100), done on November 23, 1936, gave a *three plus* reaction. Following treatment the test was *one plus, mild to moderate,* lasting 4 to 6 days. (See Fig. 4). He expects to return to "The Beaches" this summer.

Case 3

N.J., female, aged 12. Every summer on exposure this girl suffered severe and continuous attacks. Initial patch test (dilution 1/100) in November, 1936, gave a *four plus mild* reaction. Following treatment the test was one plus moderate.

Case 4

McC.D., male. aged 8. Each year this boy was taken away for his summer holidays he has had severe and practically continuous ivy dermatitis. During one attack his mother said his legs from the bathing trunk area down were one mass of weeping blisters. Another observer stated shortly after arrival he developed patches everywhere and anywhere, and that he remained "plastered" with it all summer. Initial patch test (dilution 1/100) on November 19, 1936, gave a *four plus moderate* reaction. Following treatment the test was one plus moderate to severe.

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* These cases were referred to me by Dr. A. C. Norwich. I wish to acknowledge my appreciation of his belief in the soundness of my early controls, and he felt, in consequence, safe to refer these individuals to me for treatment.

† Treatment in all four cases was continued until a final intramuscular injection of 0.5 c.c. of dilution 1/25 elicited no reaction. The total number of injections varied from 12 for Case 1 to 21 for Case 4.

VII. The Specific Antigenicity of Ether-Soluble Fractions

In this initial paper many definite observations made and conceptions now under investigation must be left out. However, some reference would seem obligatory with regard to the antigenicity of those specific substances contained in the ether-soluble fraction of not only the ivy plant but tulip bulbs, ragweed, and other similar types of vegetation. Amongst the early attempts to show the antigenicity of substances essentially non-protein in character extractable from the ivy plant is the report of Ford[3] in 1907. His experiments led him to the belief that the active substance was a glucoside, and that there was evidence of a corresponding antibody. The specificity, or rather potency, of the material used by him and supplied by Parke Davis & Co., was extremely weak as judged by its ability to induce reaction (corresponding to the patch test of today) when applied to the skin of human beings susceptible to attacks of poison ivy. In contrast to this lack of specific potency the material used by Ford was extremely toxic for experimental animals, and in these two respects his glucoside differs from the material I have called "Rholigen". The specific Rhus tox. oleo-antigen has an unbelieveably high potency as well as specificity, and at the same time has no toxicity either for the experimental animals used or for man not susceptible to dermatitis due to contact with the plant or a suitable extract.

Milford[4] in 1930 made the observation that "oil" removed from ragweed pollen caused in certain individuals a dermatitis five to twenty-one days later. Both scratch and intradermal tests were used but not the patch method. The oil was removed from the pollen with the "usual fat solvents, toluol, carbon tetrachloride, and ether". Before testing the oil was re-dissolved in a "specially prepared water-free solvent". Brown *et al.*[5] in 1931 proved by means of the patch test that the excitant was the "oil" and not the atopic fraction of ragweed. The purpose of their study at that time was "to establish an etiological relationship between pollen dermatitis and pollen oil, in other words, to prove that the pollen oil and not the pollen atopic excitant is the cause of the dermatitis". The inference of course is that if one would attempt specific therapy the "oil" in some medium should be

used. These most fundamental observations provided the essentials upon which I based my investigation of dermatitis due to contact with tulip bulbs as well as dermatitis caused by ragweed. The successful result by preventive treatment in a case of "tulip fingers" has already been mentioned,[1] and since that article I have had satisfactory results with two cases of dermatitis giving positive patch tests with the oleo-antigen of ragweed.

Brunsting and Williams[6] in 1936 report on the large total of 48 cases of sensitivity to the oil of ragweed. Their results with the intramuscular injection of ragweed oil were unfavourable in that "in nineteen of twenty-four cases in which oil treatments in varying amounts had been given, there was no relief of symptoms". They used a standard material prepared by a commercial firm.

The only conclusion from these contradictory reports would seem to be that the oleo-antigens as prepared and employed by me from the poison ivy plant, from tulip bulbs and ragweed, in so far as specificity and potency are concerned, must contain specific substances of great potency, whereas that employed by Brunsting and Williams, prepared from ragweed, did not. I group these three types of vegetation together because the same methods of preparation have thus far given me comparable and favourable therapeutic results in all three; and all three illustrate what would appear to be a new type of antigen soluble in corn oil and essentially without protein content.

Previous and subsequent to the report of Brunsting and Williams which reflects adversely upon the therapeutic value of the "oil" of ragweed a considerable number of papers have been published upon various types of extracts made from the poison-ivy plant. It is beyond the scope of this report to deal with any of these except from two points of view. Engman and Kile[7] in 1934 modified Coca's method to extract the "oil" of the ivy plant. They used the patch test on a few cases, and concluded that the active principle was contained in the unsaponifiable fraction. Treatments by injection were not attempted. Blank and Coca[8] in 1936 reported on the results of prophylactic injections of a large group of men. The material used was a preparation "extracted from poison ivy leaves with acetone and freed from chlorophyll". They state that in a previous investigation "the results of quantitative skin tests were the same after desensitizing injections as before". Obviously their preparation did not contain the specific excitant in a satisfactory state of potency. Sharlitt and Newman[9] in 1937 report upon the treatment of 74 cases during their attack. Nevertheless those in which they felt the results were beneficial, were oddly enough patch-positive, while in 6 out of 11 not benefited the patch test is reported as negative. The solvent used by them was absolute alcohol.

Thus from the standpoint of specificity and potency there would seem to be little if any similarity to the product I have named "Rholigen" and those reported upon by others interested in this subject. The bibliography cited gives an ample review of the literature.

SUMMARY

1. The ether-soluble fraction of the poison ivy plant taken up in mazola (corn) oil is innocuous to animals and man not susceptible to poison-ivy dermatitis when injected intramuscularly. This preparation has been labelled "Rholigen" (Rhus tox. oleo-antigen).

2. The potency of this oleo-antigen is such that it must be diluted for patch testing those who have had attacks of poison ivy dermatitis.

3. Following an adequate series of intramuscular injections of the oleo-antigen the skin sensitivity of selected individuals unusually susceptible to poison ivy dermatitis was reduced to a negligible degree: a degree seemingly consistent with ordinary clinical immunity.

These investigations were carried out in my private offices.

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EXPERIMENTAL GAS EMBOLISM: II. FACTORS OTHER THAN AIR AS A CAUSE OF DEATH IN SOME CASES DIAGNOSED "AIR EMBOLISM"*

By B. C. Coles, H. F. Richardson and G. E. Hall

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At post-mortem examination of fatal cases of criminal abortion gas is frequently found in the great veins and heart, and death is ascribed to air embolism. In previous work carried out on this subject[1] it was shown that surprisingly large volumes of air could be administered intravenously to dogs without fatal results. Even when injected instantaneously from 6 to 8 c.c. of air per kilogram body weight are required to produce death. If air can enter the vascular system through the open venous sinuses in the uterus it would appear logical to assume that liquids also could follow the same route. In those cases where abortion is procured through the use of intrauterine douches, air and liquid may both be present at the open uterine sinuses.

In considering the possibility of gas or liquid entering the venous system one of two conditions must be fulfilled; either the pressure within the vein must be negative or the pressure outside the vein positive. In addition there must be an opening into the vein of such a character that it will not collapse and be sealed off by these differences in pressure.

Obviously a fluid can be forced (injected) into a vein, and it is the purpose of this paper to show: (1) that *aspiration* of fluids may occur; (2) that solutions commonly used as vaginal douches are considerably more toxic than an equal volume of air.

Experimental

1. *Aspiration of fluids.*—In this group of experiments, using dogs under nembutal anæsthesia, kymographic records of respiration, heart-rate and blood-pressure were taken. The external jugular vein was exposed. It was noted that the vein collapsed with each inspiration, indicating a negative pressure within the vessel. In other dogs the abdomen was opened, and with the animal in the supine position collapse of the inferior vena cava was noted during inspiration, as low down as its bifurcation. When the head was lowered the degree of collapse became more pronounced in the inferior vena cava and less marked in the external jugular vein.

To prevent bleeding from above the external jugular vein was ligated high in the neck, and a window cut in the wall below this point. A soft rubber catheter was inserted for a distance of one inch, and its distal end attached to a water trap which clearly indicated the passage of air into the vein during inspiration. The animal aspirated sufficient air in this way to cause death. The type of death was identical with that seen in cases where air was injected intravenously with a syringe. (See Figs. 1 and 2). This experiment was repeated, immersing the end of the catheter in a solution of normal saline held just below the opening into the vein. Again, aspiration occurred with each inspiration, and fluid could be seen entering the vein.

2. *Toxicity of douche solutions.*—Solutions commonly used as vaginal douches were then investigated with regard to toxicity. Those considered were commercial phenol preparations, sodium and potassium soap, potassium permanganate, and bichloride of mercury. These were injected intravenously into rabbits with the results as shown in the table. Death within two hours was arbitrarily taken as the criterion for fatality of injections, although with few exceptions five minutes was the time limit in those cases ending fatally.

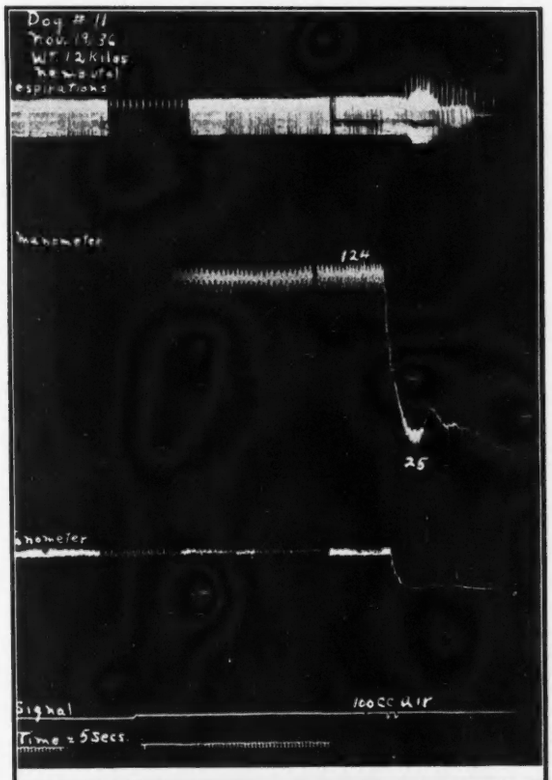
Table

Table Showing Lethal Doses of Solutions Tested.

Solution tested	*Percentage concentration*	*Lethal dose per kg. body weight*
Potassium soap (liquid green soap)	10.0	0.5 – 1 c.c.
Sodium soap (castile)	5.0	1 – 2 c.c.
" " "	10.0	0.5 – 1 c.c.
Phenol preparations (lysol, ly-septol)	0.33	Very large volumes given with no appreciable immediate effect.
" "	1.0	5 – 10 c.c.
" "	2.0	2 – 3 c.c.
Potassium permanganate	1.0	1 – 2 c.c. caused death in 20 per cent of cases within 2 to 3 hours.
Bichloride of mercury	0.1	1 – 5 c.c. without fatal results.

* The first paper in this series can be found in the *Journal*, 1937, **36:** 584.

Fig. 1



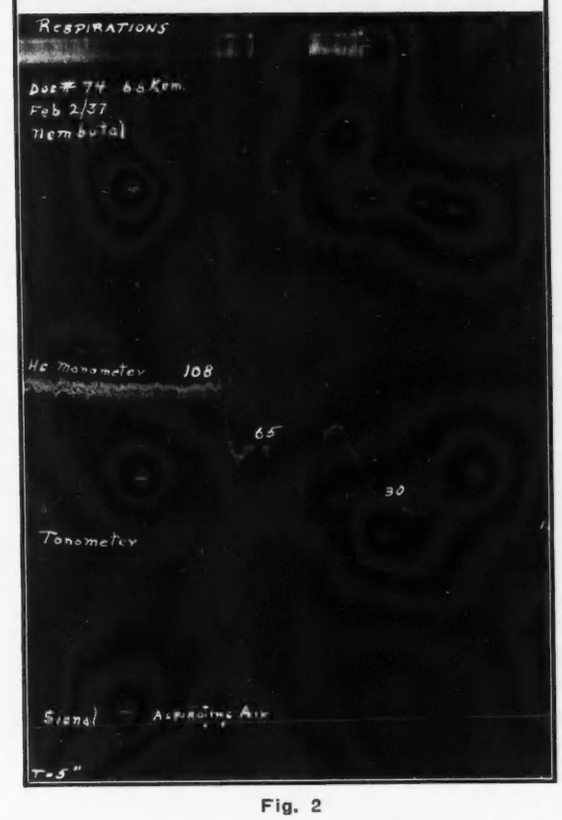


Fig. 2

Fig. 1.—Effect of sudden injection of 100 c.c. of air into the femoral vein by means of a syringe. Fig. 2.—Catheter tied in external jugular vein. Aspiration of air occurring between two signals, as labelled. This animal has aspirated an amount of air apparently equal (in c.c. per kg.) to that injected into D 11, Fig. 1. Note the similar sudden fall in blood-pressure, and the asphyxial type of death.

Thus we find that sodium and potassium soap are the most toxic in those concentrations used, with phenol preparations, potassium permanganate and bichloride of mercury showing much less severe reactions.

Having determined the relative toxicity of these solutions, they were then used in acute experiments on anæsthetized dogs, to determine if the fatal dose was approximately the same per kg. body weight. This was verified. A phenol preparation was found to be much less toxic than either sodium or potassium soap, yet in one case (dog D 76/36, 7.1 kg.) 12 c.c. of a 2 per cent solution caused death in five minutes.

In choosing solutions the percentage strength was based on what we considered was quite likely to be used by the laity. Phenol preparations are well known and concentrated solutions would not likely be used. A 10 per cent solution of either sodium or potassium soap will foam on shaking, but is too weak to form a lather. It has been shown that even in these comparatively low concentrations these soaps are remarkably toxic. It is also obvious that the all too familiar use of tablets of pure potassium permanganate might easily be duplicated in the use of much stronger concentrations of these various solutions than have been tested.

In conclusion, we have shown that gas or liquid can enter the venous system in the dog, not only by injection but by aspiration. Common douche solutions, particularly sodium and potassium soaps, are fatal (to the dog) in markedly smaller quantities than is air, and are more likely to be present in large quantities at the open uterine sinuses. Therefore we feel that the possibility of some substance other than air should be considered as a cause of death in those cases coming to autopsy following criminal abortion, even when air is found in the heart post-mortem.

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"Do not waste the hours of daylight in listening to that which you may read by night. But when you have seen, read. And when you can, read the original descriptions of the masters who, with crude methods of study, saw so clearly."—*Osler.*

QUARTAN MALARIA TRANSMITTED BY TRANSFUSION*

BY ERNEST MCCULLOCH, B.A., M.D.

Toronto

MALARIA of any sort is rare in Toronto now, apart from the occasional case which is seen in the hospitals and asylums, in which the malarial treatment of general paresis and cerebrospinal syphilis may be carried on. Even these cases of induced malaria are of the milder and more easily cured tertian type which have been carefully controlled since this form of treatment has been instituted. It must be admitted, however, that with the proper mosquito in the neighbourhood, the occasional transmission of malarial infection from hospital patients may be possible, for, without doubt, some of these paretics may get back to the association with their friends or neighbours when still harbouring a resistant form of the parasite, and the stage might well be set for a small outbreak of malaria here or there.[1]

It is to be again remembered that in these days of automobile and trailer life infected persons from the southern and southwestern states may be passing through many parts of southern Ontario where the anopheles still prevail; and malaria of any type, tertian, quartan, æstivo-autumnal, may well be thought of when physicians of these districts are brought face to face with fever of unexplained origin, for in the medical history of Upper Canada malaria was a well-known foe,[2] and it was long suspected that the pernicious type of malaria found along the Lake Erie shore was brought there by the voyageurs and explorers as they returned from their trips to the south by way of the Mississippi.

The disappearance of this pernicious malaria from southern Ontario has been witnessed by older practitioners,[3] and it is interesting to note that this disappearance has taken place in face of the fact that the anopheles still prevail in many districts along the Lake Erie shore and even in the neighbourhood of Toronto, more particularly now in the country districts, since with the growth of cities and towns and the blocking-up and diversion of streams and marshes, the culex seems to replace the malaria-carrying mosquito. The changes in the routes of travel and the introduction of quinine, did much no doubt to take away from the mosquitoes' source of supply, while again it is well recognized that in the cooler climates of the north malarial parasites do not find their most congenial surroundings. To cultivation and drainage, moreover, must be given some credit in the ridding of our part of the country of the malaria which at one time amounted actually to a scourge.

As far as can be gathered from the scattered clinical records the form of disease prevalent in both the early and later colonial days was probably the common tertian. Cases due to the quartan parasite must, however, have been occasionally met with as long as travellers were bringing their infection from the south. Since the study of blood in malaria was only developed on this continent in the late 80's and early 90's, and since malaria itself was disappearing from Ontario by this time, we have few pictorial proofs of the relative frequency of the tertian and quartan parasites in the blood of malaria patients in this part of the world. By analogy with conditions in the southern States, one may assume that the quartan parasite would only rarely have been met with in Ontario, hence part at least of the interest we have taken in the case we are reporting.

A no less interesting detail of the case is that the malarial infection from which the patient suffered seems to have been transmitted by a transfusion of blood from her father. Equally interesting in this connection is the fact that her parent's malarial infection must have dated back to his residence in Roumania 25 years ago. The danger then of transmitted malaria in the process of transfusion must surely be existent in malarial countries, for a donor free of symptoms for 20 to 25 years would usually be considered as malaria-free. One may suggest that in taking the amount of blood necessary for transfusion, the splenic sinuses and bone marrow were tapped and drained, and again that in our unsuitable climate the malarial parasite

* Read before the Wellesley Hospital Clinical Society on December 9, 1936.

harboured by the donor had been hiding in the spleen or bone marrow. One may even fancy that the parasite assumes some special form for its protracted hibernation.

That such a resting form is assumed, however, has not been demonstrated, but that malaria may lie dormant for years, during which time the parasite is not in evidence in the surface blood is a well recognized fact, particularly in the case of quartan infections, and one may state with a reasonable assurance that the quartan parasite met with in our case had its origin in Roumania, was resistant to treatment (if treatment had seemed necessary), was driven into the spleen and bone marrow by the unfavourable Canadian climate, remaining there viable and active till caught in the vigorous transfusion flow. Recrudescence or relapse of malaria after years, may frequently be precipitated in a patient by injury, operation or other illness. This capacity for hiding during unfavourable circumstances is shown by other parasites, to wit, the nocturnal filaria.

CASE REPORT

The case in hand was that of a young married woman delivered in the Women's Colloge Hospital on September 1, 1936. There had been no history of preceding malaria, no recent exposures to a possible source of infection. A transfusion was deemed necessary immediately after the confinement and was given on the same day. Her father was considered a suitable donor. Twenty-six days after the transfusion fever was noted, and in a few days this fever had assumed an intermittent course associated with chills. All the various accidents associated with labour were considered, and all the various infections which might be looked for in this part of the world were considered, but with negative results. The fever and chills occurring now every fourth day were associated with a progressive anæmia and with a low white blood count. After two weeks of an illness during which innumerable blood examinations were made the patient fell into my hands. One noted the absence of signs suggestive of septic infection, the comparative well-being of the patient on the fever-free days, and, on viewing the temperature chart, one's suspicions were aroused by the regularity of the appearance of recurring paroxysms of chills and fever. Blood was taken to be examined for malaria on the 51st day after the transfusion, and both myself and Dr. McClure, from the Provincial Board of Health, had little difficulty in finding numerous malarial parasites of the quartan type. Pictures of this have been reproduced below, though one regrets that expense prevents the printing of Dr. McClure's excellent coloured plates. There was little else in the general examination of the patient. A slight enlargement of the spleen was noted, and, as might be expected after a number of chills, a very distinct secondary anæmia.

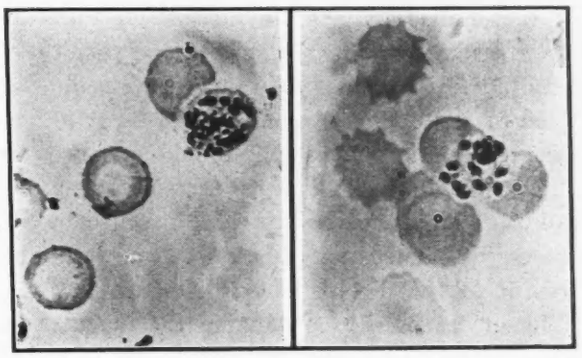
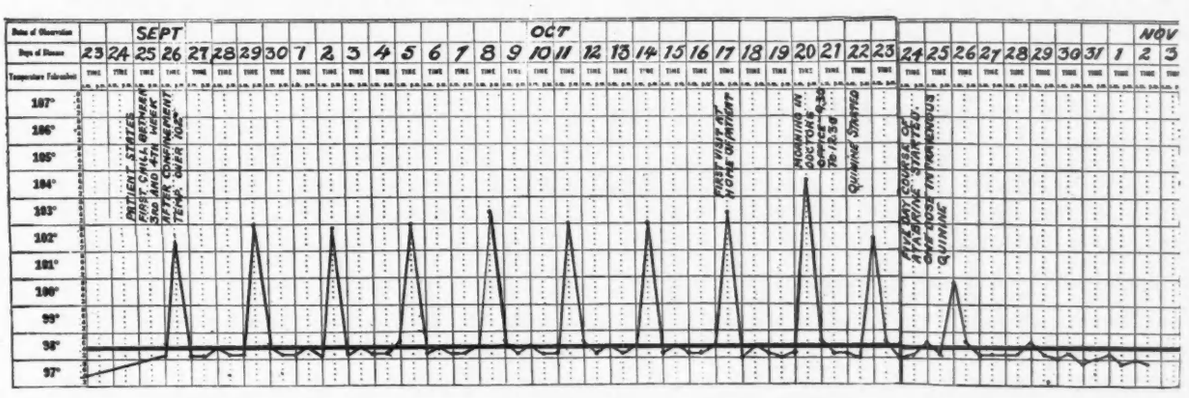


Fig. 1 Fig. 2

Fig. 1.—Mature forms of the quartan type showing reduction of size of red corpuscle and the curious granular pigment. **Fig. 2.**—Segmentation complete and the merozoites discharged from the red corpuscle.

The fever and the severe shaking chills disappeared after five doses of quinine given intravenously. In order to complete the cure by acting upon the sexual forms of the parasite the quinine was followed by a five day's dosage of atebrin, one of the newer synthetic preparations now in use. By the third day of treatment no parasites could be found in the blood, and one month later the patient reported as free from any suggestion of fever or associated disorder.

The accompanying chart shows well the typical quartan picture as we have reproduced it from our records. Unfortunately it was not possible to make a four hourly chart which would show how much more prolonged are the paroxysms of malaria than are those of the acute septic processes. The prompt effect of quinine is seen in the disappearance of all fever in a matter of three days, and one hopes that with the quinine and the added atebrin all in-


SEPT
OCT
NOV
PATIENT STATES FIRST CHILL WEITHERS 3RD AND 4TH WEEK AFTER CONFINEMENT TEMP. OVER 102°
FIRST VISIT AT HOME OF PATIENT
MORNING IN DOCTOR'S OFFICE 4.30 TO 12.30
QUININE STARTED
AFTER MAY COVERED 5 DAYS OF ATEBRINE GIVEN QUININE INTRAVENOUSLY

fection has been eradicated. Of this, however, we have no absolute proof without careful examination of material obtained by puncture of the spleen. This latter procedure, however, is one not unassociated with danger.

Various other matters may be briefly touched upon in discussing this most interesting case. One is the time necessary for the development of the malaria after the massive inoculation given in transfusion. It is probable that there were but few parasites present in the circulating blood of the donor, for none could be found in careful examination of the stained smears. As suggested, it might not be till the splenic sinuses and the bone marrow were being drained in the process of transfusion that parasites would be present in the flowing blood. Only a few c.c. of blood are used in producing the inoculation malaria in the treatment of general paresis, and, depending probably on the number of parasites present, one finds that the chills and fevers may develop in anywhere from 7 to 30 days. These figures are taken from Dr. L. D. Rudolf's interesting publication on inoculation malaria. In our patient the first signs of fever seem to have been recorded at about the 26th day. Unlike many of the cases of quartan infections, judging from the temperature chart and from the parasites as we saw them, the patient had only acquired what would be called a single quartan infection, and in the microscopical slides examined, and here reproduced, all the parasites are within a few hours of being of the same age. Those familiar with malaria recognize that infection with multiple groups of organisms occurs, probably as a result of bites by different mosquitoes at various times. With two groups of organisms segmenting in sufficient numbers, a so-called double quartan infection may be seen, in which chills occur on two successive days followed by one day of freedom from chills and fever, and then again chills and fever in succession for two days, while if a third active group of quartan parasites are in the patient's blood there will be chill and fever every day, just as we see the daily chill and fever with a double tertian infection. It is not uncommon in quartan infections, however, to find parasites of varying ages but not present in sufficient numbers to give the patient the characteristic picture of a double or triple quartan infection.

Another matter is the risk of transmitting malaria in the process of transfusion. Such transmissions have been recorded from time to time in the past, must of a certainty happen more than occasionally in malarial countries, and are being seen to occur here and there in countries usually considered free from malaria when some donor who has forgotten his malarial history is used for the transfusion. The literature on the subject is growing and one may refer to an early article by Gubb[4] in 1919, and to another by Oehlecher[5] in 1920, who states that in the case reported by him the donor was unaware of ever having had malaria. In our own case, we have stated that infection must have occurred 25 years previously, yet, again, the woman's father insists that he had no recollection of ever having been infected. Decourt[6] records an instance in which the donor was infected during the process of transfusion, which suggests that the receiver must have been heavily infected at the time of the transfusion. Other isolated case reports of transmission of malaria by transfusion are those by Stein[7] and by Jankleson,[8] in 1932 and 1931 respectively, while one is interested to find that we have been preceded in the discussion of the matter by Cadham,[9] of Winnipeg, in his report of a case in that city in 1936.

Much more striking than the occurrence of these isolated cases, however, is the report from China in March, 1936, by Wang and Lee,[10] of the transmission of benign tertian malaria in no less than 54 cases during a 10-year period from 1925 to 1935. The finding of enlargement of the spleen is looked upon by these authors as more likely to be of help where the question of chronic malaria is being considered, since parasites in the blood will only rarely be found in donors who are not showing symptoms. A matter of further interest in the report from these two authors is that in one of their cases both malaria and relapsing fever were transmitted by the transfusion.

In conclusion, one may say first that the quartan type of malaria has probably only rarely been noted as occurring in Upper Canada. Next, that the ability of the malarial parasite to remain hidden, yet living and actually dangerous, for as long a period as 25 years has been strongly suggested by the history of our case. Finally, the danger of transmission of

malaria by transfusion is well recognized in malarial countries and should be regularly thought of even in the temperate climes, if the donor gives the history of having lived in countries where malaria is known to be prevalent.

The author desires to express his sincere gratitude to Dr. Norman Gwyn of Toronto for his inspiration and assistance in preparing this report.

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SOME CHANGING VIEWS ABOUT ŒDEMA AND DIURESIS*

BY HENRY A. CHRISTIAN

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ONE of the very pleasant things, as one grows old, is retrospection, recalling to mind earlier views about various subjects, comparing past with present ideas. Thus one relives the experiences associated with the progress that has occurred during his lifetime association with his chosen field of activity. Of late I have been doing this myself, stimulated by reading stenographic reports of lectures given to earlier Harvard medical students. Twenty-eight years ago, as successor in the Hersey professorship of the Theory and Practice of Physic at Harvard to Dr. Reginald Heber Fitz, the discoverer of appendicitis, I began giving didactic lectures in medicine to students. Recently reading notes of these lectures has aroused in me an interest in the changing views about œdema and diuretics of the last three decades. Perhaps something of this may be of interest to you; at any rate I hope so.

Nephritis, œdema and diuretics long have been of great interest to me. In my early clinical days I spent considerable time in the experimental production of nephritis in rabbits, studying the changes so produced and testing out effects of diuretics. Ever since then I have been watching patients with nephritis, and I and my associates and students have been studying various problems presented by them. This has made me interested in the many studies coming from many laboratories and clinics in these intervening years. Œdema long had been recognized as a complex and not well understood process, whether associated with Bright's disease or cardiac insufficiency; complex it certainly is, and even now its mechanism is far from well understood. That it was complex and but poorly understood was my instruction in 1908-9 to medical students, just as it is today. As to Bright's disease, then I was telling them that œdema occurred in both acute and chronic nephritis, but not in every patient with these conditions; that usually it was very slight in chronic interstitial nephritis, while, as a rule, very marked in chronic parenchymatous nephritis; that it was apt to be much less marked in acute nephritis; that, notwithstanding these usual associations, there was no definite relationship between a given anatomical change in the kidney and the occurrence and degree of œdema. Then the terminology of nephritis was different from that of today. Modernizing this terminology, this statement as to œdema still holds good. Chronic parenchymatous nephritis now is called chronic glomerular nephritis or even nephrosis; the dominant lesion is in the glomeruli; here œdema is apt to be marked. Yet, as pointed out then, not always will there have been œdema during life when autopsy reveals proliferative lesions in the glomeruli.

* An address delivered at the Annual Meeting of the Royal College of Physicians and Surgeons of Canada, at Ottawa, on October 3, 1936.

Conversely, until very recently glomerular lesions have been denied as occurring in that form of Bright's disease in which œdema is most prominent, so-called nephrosis. I long have held the view myself that glomerular damage was a chief factor in the nephrosis syndrome; more and more this view has been accepted by pathological histologists, able by special technique to demonstrate changes in the glomerular structures. I myself, years ago, described a hitherto unrecognized glomerular lesion in experimental uranium nephritis in which the glomeruli had been supposed to be normal; uranium nephritis is the one form of experimental nephritis associated with œdema.

Another theory of the mechanism of œdema of the 1908-9 period was that of hydræmic plethora. This was discussed by me, it being pointed out that many observers had failed often to demonstrate hydræmia, while others found that it followed, rather than preceded, the appearance of œdema, this suggesting that it was part of, rather than the cause of, the œdema process. Still, today, this last concept seems the more likely.

In 1908-9 many believed that sodium chloride played a dominant part in producing the œdema of renal disease. Chloride retention often could be demonstrated in nephritis, but not always was it accompanied by œdema. The dry salt retention of chronic interstitial nephritis was recognized. In the clinic in some patients decreasing or increasing the salt content of the diet did decrease or increase the œdema; this was found, however, to be definitely unusual. Obviously something more than salt retention was necessary to produce œdema. This led me to caution the students against prolonging a very salt poor diet in their œdematous patients, when no diuresis resulted, since such a diet was unpalatable and salt deprivation was inimical, if not actually injurious, to them. The same viewpoint was taught with regard to rigid restriction of the fluid intake. Cases were cited to show that increasing the salt or water content of the diet often actually increased the urine output in these patients; at times each might be regarded as diuretics.

What then was regarded in 1908-9 and in the next few subsequent years as the most acceptable explanation of renal œdema? It was increased permeability of the small peripheral vessels, associated with decreased permeability of the kidney to water, both caused by some sort of toxic substance causative of the nephritis. With this, variations in osmosis from changes in salt content and disturbances in water balance took place and were contributory factors. The evidence in favour of this theory was found chiefly in animal experimentation. These experiments I discussed at length before the class. It was pointed out that uranium nitrate, among substances used to produce experimental nephritis, was the one that at times caused an associated œdema, and that there were differences in renal response to certain stimuli from that in kidneys damaged by other substances unassociated with œdema formation. It had been found that, if the kidney was damaged by a non-œdema-causing substance, then œdema would follow if another substance, such as snake venom, known to injure blood vessels, was given in addition, though snake venom by itself would not cause œdema. Many years ago it had been shown that, although an excess water intake by itself would not cause œdema, œdema would appear where a mild local irritant was applied to the skin. In all such experiments œdema was more evident, if excess water and excess salt were given.

This explanation, as just given, was applied in explanation of the œdema of both acute and chronic nephritis. Today we believe that this is the best explanation of the œdema of acute nephritis. Of the œdema of chronic nephritis at present we regard lowered osmotic tension due to decreased plasma protein, and especially decreased plasma albumin, as the main causative factor. No reference was made to this possibility in 1908-9 by me. Apparently the work of Starling, published in 1896, on the relationship of colloid osmotic pressure to fluid exchange in the body had made no impress in the clinics. Even fourteen years later, although Starling had very fully discussed this possibility in his Herter lecture of 1909, almost no importance was attached to lowered plasma protein as a cause of œdema by Loeb[1] in his extensive reviews of investigations of the mechanism of œdema, Loeb saying, after discussing it at some length, "According to our present knowledge it would be impossible to consider the influence of proteins as the preponderating factor." Two years later McLean[2] gave decidedly more im-

portance to this cause, though he pointed out that "There may be marked changes in the amount of œdema without any demonstrable change in the osmotic pressure of the proteins." This explanation of œdema scarcely was utilized in the clinic until much later, even though Epstein[3] in 1922 published his study of nephrosis in which he emphasized this cause of the œdema.

The œdema of cardiac insufficiency, though complex, in 1908-9 was regarded as the result chiefly of increased intracapillary pressure; the result of changes due to poor circulation and the effect of gravity making the œdema appear first in dependent parts were emphasized then. Increased vascular permeability due to poor nutrition from poor circulation was considered an added factor in its mechanism. These views are not very different from those held at present.

In 1908-9 students were told that the œdema of chronic interstitial nephritis in the main was due to cardiac insufficiency resulting from associated hypertension, arteriosclerosis and heart hypertrophy, with resultant myocardial insufficiency. This would be expected to respond to bed rest and digitalis, and such treatment was advised to be used as a therapeutic test of the cardiac cause of the œdema—instruction certainly sound in 1936.

Early in my teaching career I was teaching that diuretics were contraindicated in the treatment of acute nephritis, a view justified by our observations that all diuretics, even so bland a one as water, tended to shorten the lives of rabbits with acute uranium nephritis. Furthermore, discontinuous, rather than daily, dosage of diuretics was advised on the basis of observations both in the clinic and the laboratory that renal fatigue occurred after a diuresis, and better effects were produced if a rest period for the kidney was provided.

In 1908-9 saline purgation and sweat baths were recommended as diuretic processes, the last soon to be abandoned and the former no longer recommended, over a period of many years. Refrigerant diuretics, the tartrates, citrates and acetates of sodium or potassium, were advocated for slighter degrees of œdema. The use of the stimulating diuretics of the theobromine and theophyllin groups then was advised; numerous forms were discussed, theobromine sodio-salicylate (diuretin), theocin (synthetic theophyllin), theophyllin sodio-acetate (soluble theocin), theobromine sodio-acetate (agurin), etc. A few years later the students were told frankly that none of these diuretics gave satisfactory diuresis in renal œdema, though effective in cardiac œdema, and that, if good diuresis was obtained, in all probability cardiac insufficiency, perhaps unrecognized, had been the chief cause of the œdema.

No mention twenty-seven years ago was made of mercurial diuretics. Calomel as a diuretic, as used at an earlier date, seemed to be out of fashion; modern mercurial diuretics had not been introduced. Novasurol was introduced as a diuretic in 1920, and its use rapidly became very general; in 1927 I was describing it as our best diuretic. Salyrgan was introduced in 1924 and more recently mercupurin. Within this year the two latter have been made available as suppositories effectively diuretic. These mercurials, especially the last two, are effective in both renal and cardiac œdema. For a considerable time we were fearful of using the mercurials in a patient with nephritis, since mercury is known to damage the kidney severely. However, careful trial gradually demonstrated their entire safety in that form of nephritis in which renal function was undiminished except for salt and water excretion, and in which œdema, as the rule, is very marked, namely in the nephrosis syndrome, as I prefer to call it, regarding it as a form or stage of glomerular nephritis.

The mechanism of action of the diuretics is not well understood. Two general views have prevailed; (1) that their action is extra-renal and (2) that their action is directly on the kidney. The latter view increasingly has been supported by experiment and clinical observation; for certain diuretics it seems proved that the action is a direct renal one. This does not mean that extra-renal factors play no part, but rather a subordinate part. Among various proofs of the direct action of diuretics on the kidney a very striking one is that of Govaerts, showing that novasurol given to an animal would continue its diuretic action after the kidney of this animal had been transplanted into an animal that had received no novasurol. Bartram showed in my own laboratory that certain diuretics, if injected directly into one renal artery in a small dosage, would cause a

diuresis from that kidney and not from the other, while in larger dosage both kidneys would show a diuresis, and in still larger dosage the kidney receiving the diuretic directly would have a lessened urine output, in contrast to that of the other kidney, all indicating a direct action of the diuretic on the kidney.

Much of what I have been discussing is directly applicable to the use of diuretics in the clinic. Much of such application you understand, and time does not permit me to elaborate now on this more practical side of the problems of œdema and diuretics as we understand them today.

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A PLEA FOR CONSERVATISM IN THE USE OF CÆSAREAN SECTION

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THE purpose of this paper is to stress the dangers of the growing, widespread, indiscriminate use of Cæsarean section and to make a plea for more conservative and skilful management of obstetrical difficulties.

The operation of Cæsarean section is one of the oldest of which there is any record.[1] It is mentioned in the Talmud, and it is known that Numa Pompilius, consul of Rome, passed a law to the effect that the uterus of any dead or dying pregnant woman should be incised to save the baby. He did this in an effort to prevent the falling birth rate. The operation was limited until the 16th century to women who were moribund or dead. In 1500, Nufer, a swine-gelder in Switzerland, successfully performed the operation on his own wife, and from that date we begin to find records of occasional cases, although the mortality was prohibitive.

In 1877, Porro introduced the procedure of removing the uterus and eventrating the stump. This resulted in a marked reduction in mortality. The danger was still so great, however, that Harris, in 1890 (quoted by Rosensohn[2]), came to this startling conclusion: "It is safer for a mother to be gored by a bull and have the baby born so than by Cæsarean section". The cases reported in which women had delivered their children as a result of being eventrated by a bull showed a 44 per cent maternal mortality, whereas, the death rate due to Cæsarean section at this time was still 52 per cent.

In 1882, Sanger advocated suturing of the incision in the uterus. This led to a still greater reduction in the number of maternal deaths, and marks the beginning of the commonly accepted present technique. In 1906 Frank advocated the extraperitoneal method of approach. Since that time there has been little advance except for the gradual increase in the proportion of low cervical as compared with high sections. Corresponding with this improvement in technique, the indications for Cæsarean section have broadened until now there is scarcely an obstetrical complication for which this procedure is not recommended. Its incidence is steadily increasing. Nevertheless, the operation still retains a most unenviable reputation for high morbidity and mortality, the reason being inherent in the very nature of the procedure. Necessarily, the operation is often performed on patients who are not the best risks. The indications may be toxæmia, hæmorrhage, heart disease, or the patient may be exhausted from a prolonged labour and actually or potentially infected. Such conditions, of course, add greatly to the dangers of any operation. The incision in the greatly enlarged, soft, and highly vascular uterus results in a loss of blood that is conservatively estimated to be more than five times as great as that following normal delivery from below.[3] The baby, covered with vernix caseosa, the placenta, membranes, amniotic fluid, meconium and blood are then all removed through the peritoneal cavity. No other operation in abdominal surgery so exposes the peritoneum. The uterine cavity, filled with blood and communicating at its lower end with the infected vagina, serves as an excellent culture medium for bacterial growth. The infection can then readily spread through the uterine incision to the peritoneum or by means of blood vessels or lymphatics to various parts of the body. As a

result of all these factors, patients frequently die of shock, hæmorrhage or infection. The low cervical section would appear to be safer in infected cases but even it has a high mortality rate.

Plass (quoted by Schwarz and Paddock[4]) estimates that there are 25,000 Cæsarean sections in the U.S.A. each year, with a maternal mortality of about 10 per cent. This is at least twenty times as great as the maternal death rate for vaginal deliveries. There is excellent evidence to show that about three-quarters of these sections are not justified. In other words, there are about 20,000 unnecessary Cæsarean sections in the U.S.A. each year, from which 2,000 mothers die.

The Committee of the Ministry of Health in England recently made this report: "The Committee's observations lead them to believe that in some cases there may be a tendency to resort to Cæsarean section as a treatment for the complications of labour, perhaps without due consideration to other methods of obstetrical treatment."

The New York Academy of Medicine Committee, in its report on maternal mortality in New York City in 1933 concludes as follows: "The data reveal an excessive use of Cæsarean section, and as a result a great increase in maternal mortality". "A sharp reduction in the number of Cæsarean sections performed is to be strongly recommended. Only by definitely narrowing of its use to the legitimate occasions demanding it, as well as by the provision of capable operators, can a decrease in these deaths be achieved."

Holland, in *The Lancet*, in 1935, states: "The increased opportunities given to local practitioners who may possess neither the requisite judgment nor skill in performing Cæsarean section have resulted in a remarkable increase in the number of these operations."

Recently, in a series of over 3,000 cases of Cæsarean sections, performed in five large maternity hospitals in the British Isles and in the borough of Brooklyn, 63 per cent were done for contracted pelvis. Banister[5] makes this comment: "This is surely an unwarranted slur upon modern feminine physique." In this series of cases there was a 6.6 per cent maternal mortality, or 1 death in 16, as compared with a maternal mortality of 0.45 per cent, or 1 death in 200 for vaginal delivery. In the very best hands in English hospitals the death rate from Cæsarean section is 5.8 per cent.

A recent bulletin of maternal deaths, from the Department of Labour in United States, showed that 7 per cent of all maternal deaths were due to Cæsarean section, 24 per cent of all maternal operative deaths were due to Cæsarean section, and in 44 per cent or almost half of the patients who died from Cæsarean section, the indication for operation was toxæmia.

Lull,[6] in 1933, found that the average maternal mortality in U.S.A. following Cæsarean section was 6.7 per cent, varying from 5 to 10 per cent in different localities. The morbidity with the classical operation he found to be 41 and with the low cervical section 38 per cent. Gordon,[7] in 1934, reported a maternal mortality of 11.4 per cent in Cæsarean sections done for breech presentations. O'Connor,[8] in 1934, reported a series of 436 sections with a gross mortality of 4.6 per cent. In this series the classical operation carried a 4 per cent and the cervical a 5.3 per cent rate. Fifteen per cent of the deaths occurred in clean, elective, non-complicated cases, in good condition.

De Lee,[9] in 1934, stated: "I must, however, warn against the growing misuse of a noble operation. The mortality from it in U.S. is at least 6 per cent, which is frightful and something must be done about it. In some places the mortality is over 10 per cent, and we wonder if we have not wandered too far from old friend 'watchful expectancy'. Also, where have the real obstetricians gone? As soon as the doctor is presented with a complicated knot in obstetrics to untie he simply cuts it."

Trillat,[10] in 1933, reported 110 cases of low cervical section with a maternal mortality of 7.2 per cent. In this series there was a 3 per cent maternal mortality for clean cases and a 28.5 per cent maternal mortality rate for infected cases. De Lee again is drawn to comment: "I learn from these figures that even the low section has a high mortality in infected cases, and that perhaps we should fall back on our dishonoured friend, craniotomy."

Plass,[11] in a survey of Cæsarean section in the State of Iowa from 1930 to 1932 inclusive, found that the maternal mortality rate was 7 per cent and that 1 per cent of all the women in the state were delivered by this operation. In urban centres from 2 to 7 per cent of all deliveries are by Cæsarean section,[12] the average being about 4 per cent or 1 out of every 25 deliveries. It is evident from these and many other figures that could be quoted that Cæsarean section, even when done by skilled operators, carries a very great risk, and that fewer of these operations should be performed, especially since far too many are done for non-valid indications.

It is true that in certain isolated series of reported cases the maternal mortality rate with low cervical section has been considerably less than the figures quoted above. Thus Daily[13] reports 500 cases at the Chicago Lying-in Hospital with a maternal mortality rate of only 1 per cent; 381 cases at the Michael Reese Hospital carried a rate of 2.1 per cent;[14] R. J. Heffernan[15] reports 150 cases without a single death; and H. J. Stander[16] presents 153 cases with only 1 death. The higher mortality rates previously mentioned approximate much more closely the actual maternal mortality from Cæsarean section as performed indiscriminately throughout the country, and when compared with the lower figures make it very obvious how much improvement can be achieved by limiting the operation to properly selected cases and skilful operators.

It is evident that no estimate of the dangers of Cæsarean section can be complete without a consideration of the immediate and late morbidity as well as the mortality. For each patient who dies, there are many who barely escape a fatal outcome, and still more who suffer late complications that are often troublesome and incapacitating. Following a review of the immediate and remote effects of Cæsarean section at Jefferson Medical College Hospital, Montgomery[17] makes this statement: "The findings convince the author that Cæsarean section, in its many potentialities for danger, occupies an unparalleled position among abdominal

operations.'' The immediate complications include infected incisions, uterine infections, pulmonary complications, septicæmia, peritonitis, intestinal ileus, thrombophlebitis, urinary tract infections, anæsthetic sequelæ, and other conditions too numerous to mention. Later on, pelvic adhesions, ventral hernias, lower abdominal pain, chronic vesical symptoms, and chronic intestinal obstruction frequently cause trouble.

It is important to remember that Cæsarean section greatly increases the risk of the next pregnancy, and that the maternal mortality rate rises with each succeeding section. In each case, therefore, before deciding upon Cæsarean section, it is necessary to consider not only the immediate dangers but the likelihood of late complications in the mother and the increasing possibilities of mortality with subsequent pregnancies.

Everyone agrees that Cæsarean section has a place of importance in obstetrical practise. Even the most conservative obstetrician will admit that this operation is often not done when it should be, but there is none so radical as to deny that it is done far more often when it should not be. There are several reasons for the increase in Cæsarean sections in this country. First, might be mentioned the development of the surgical outlook, the contempt for nature with her more deliberate, painful, but infinitely safer technique. The second factor is ignorance, the failure to appraise the exact conditions and indications. It often requires a great deal of obstetrical experience and judgment to determine the best method of delivery in a difficult case, and this experience is frequently sadly lacking in the operator. It is for this reason that the practice of obstetrics should be in the hands of obstetricians and not surgeons. A third factor is the increasing value of the life of the baby due to the falling birth rate. It is well to remember that it is better to lose an occasional baby than an occasional mother. For every ten Cæsarean sections that are done in the interest of the baby, roughly, one mother is lost. It is very doubtful if the number of babies saved by this procedure justifies such a risk, particularly since published reports indicate that the fetal and infant mortality following Cæsarean section is much higher than after vaginal delivery. A fourth factor that is extremely important in leading to an increase in the number of Cæsarean sections is the host of articles that are being written by prominent obstetricians enthusiastically advocating Cæsarean section for every obstetrical complication imaginable, from breech presentations to hydrocephalus. Their arguments seem so convincing and their results so enticing that one is tempted to take their advice and try this operation, instead of practising sane, conservative obstetrics on the next difficult case that comes along. Unfortunately, the results are not always so good as those obtained by the original proposers.

The indications for Cæsarean section are either absolute or relative. Absolute indications exist when it is impossible to deliver the baby from below, even by resorting to craniotomy. Such a situation is very rare and only occurs where the true conjugate diameter of the pelvis is less than 6½ cm. or when there is a tumour obstructing the pelvis. Under these conditions there can be no argument against Cæsarean section. It is in connection with the relative indications that there is so much difference of opinion. Some of the more common of these indications will be considered, here.

Placenta prævia.—Many obstetricians advocate Cæsarean section for all cases of placenta prævia, but certainly the great majority of such patients can be delivered quite safely from below with a very low maternal mortality rate. It is true that Cæsarean section has a limited field in the treatment of central placenta prævia in primigravidæ, but placenta prævia is more common in multiparæ and the central type is relatively infrequent.

Accidental hæmorrhage.—Irving[18] reported 269 cases of accidental hæmorrhage. Those treated by Cæsarean section had a death rate of 15.7 per cent. In cases of similar severity treated conservatively the maternal mortality was only 7.1 per cent, less than half. The tendency throughout the country is to do a Cæsarean section on any woman past the sixth month of pregnancy the moment she loses some blood. A very prominent obstetrician has advocated this operation for all women who begin to bleed even in small amounts during the first stage of labour. If this teaching were followed there would be countless more unnecessary sections and unnecessary deaths. There are cases of placenta prævia and of accidental hæmorrhage which indicate Cæsarean section, but most

of them can be treated conservatively with more safety.

Eclampsia.—It must be admitted that any patient with hypertension, nephritis, convulsions and, perhaps, coma is a very poor surgical risk. To subject such a patient to Cæsarean section is to court disaster. The shock of Cæsarean section in an eclamptic patient, even when done under local anæsthesia, and the decreased resistance to infection which such a patient has, practically precludes its use, the mortality rate being in the neighbourhood of 20 per cent. Besides, the conservative treatment of eclampsia is conceded the world over to yield better results. We can, therefore, conclude that Cæsarean section is practically contraindicated in eclampsia, although its use may be occasionally justified in the non-convulsive toxæmias.

Heart disease.—The primary consideration in heart disease is to determine the type of delivery which will impose the least shock and strain on the mother. If the patient is a primigravida with evidence of disproportion so that a long, difficult labour can be expected, sometimes a Cæsarean section is justified, but it is well to remember that this in itself carries more shock and strain than most prolonged labours. Moreover, it has been found that patients with moderate cardiac decompensation often stand the ordeal of labour very well. They frequently have short, easy labours, and usually take general anæsthetics well. In this connection it is worth while mentioning that one is never justified in doing a Cæsarean section simply because it provides an easy opportunity for sterilizing the patient at the same time. There can be no excuse for subjecting a patient to a risk of a 7 per cent maternal mortality to carry out a procedure which can be performed a few months later with a risk of considerably less than 0.5 per cent.

Tuberculosis. — The same arguments apply here as in heart disease. One is only justified in subjecting a tuberculous patient to such a serious operation as Cæsarean section when it seems inevitable that delivery from below would entail an extremely severe and prolonged labour. By the proper administration of fluids and sedatives during the first stage and the use of forceps early in the second stage, these patients can usually be carried through with very little trouble. It is important to realize that the medical complications of pregnancy do not in themselves constitute an indication for Cæsarean section. The operation should be reserved for only those cases in which there are, in addition, sufficiently good obstetrical grounds to justify it.

Contracted pelvis and cephal-pelvic disproportion.—This is the commonest excuse given for performing most of the unnecessary Cæsarean sections today. At the University of Iowa, between 1926 and 1935,[19] there were 5,446 deliveries and in only 12 of these, or 0.2 per cent, was it found advisable to perform Cæsarean sections for this reason. As a matter of fact, there were only 67 done altogether during that period and 42 of these were done because of previous sections (most of which had been unnecessary). This means that there were only 25 primary Cæsarean sections in 5,446 deliveries at Iowa in the past ten years, an incidence of less than 0.5 per cent. This conservatism reflects itself in an enviably low maternal mortality rate, and the fetal mortality rate is no higher than in other centres where Cæsarean section is much more frequently used. It would seem that whenever the head does not engage early in labour or before labour in a primigravida, or whenever the progress is unduly slow and it appears that there is going to be some difficulty and special skill required to deliver the patient from below, the attendant flees to Cæsarean section as the easiest way out. He does not realize that in so doing he is greatly adding to the maternal risk, often quite unnecessarily. As Langrock[20] points out: "The attendant's decision as to whether a patient with disproportion should have a Cæsarean section depends on; (1) his obstetrical knowledge and experience or lack of such; (2) his skill in vaginal delivery or lack of such; (3) his courage and patience to wait and deliver from below; (4) his willingness to sacrifice time and strength in the interests of the patient." The fact remains that most patients with borderline pelves and disproportion can be delivered by the vagina, often with surprising ease. Certainly the fact that the head is floating at the onset of labour in a primigravida, no matter what the presentation, does not justify the attendant becoming panicky and resorting to Cæsarean section. It must be remembered that a true test of labour requires

at least two hours of strong pains with the cervix fully dilated. It is only after such a trial that one can say with any degree of assurance whether the child will come through in cases of questionable disproportion.

How many of us have encountered that very ludicrous, if it were not so tragic, example of poor judgment that occurs when a patient who has had a prolonged, difficult labour is being prepared for Cæsarean section and she manages to deliver the baby from below before the operation can be begun? If she had only been considerate enough to wait another twenty or thirty minutes she would have had a Cæsarean section, and some surgeon would have prided himself on his rare good judgment in saving the mother's or the baby's life. We have seen four such cases, and many practitioners have had similar experiences. It is certainly true that for every patient that successfully eludes the knife there are tens and hundreds who are not so fortunate and are unnecessarily exposed to the great risk which Cæsarean section entails. It requires a great deal of judgment and skill to carry a patient through a prolonged difficult labour, and Cæsarean section offers such an easy way out. But it is for the development of just such skill and judgment with its attendant lower maternal mortality and morbidity that this paper is making an earnest and sincere plea.

Uterine inertia, rigid cervix, and lack of progress.—This is another group of indications that are very often called upon to justify Cæsarean sections, the great majority of which are certainly not indicated. It is a well known fact that the duration of the first stage of labour is variable, from a few minutes or hours to days, depending on the nature of the uterine contractions and other factors. The cervix, except when it is badly scarred from previous operations or is the seat of some disease or tumour growth, will almost always become fully dilated if given time and if the patient is really in labour. It must be remembered that many women have very severe abdominal pains accompanying regular uterine contractions and are not in true labour at all. Almost the only way that we have of knowing whether a woman is having true or false pains is by noting whether the cervix effaces and dilates. There is no doubt that many Cæsarean sections are done on women who were never truly in labour, the excuse being that in spite of good pains for twenty-four hours or longer the cervix did not efface or dilate.

In the investigation of the Cæsarean sections throughout the state of Iowa, referred to above, it was interesting to note how very often the surgeon justified operation on the grounds that the patient was in labour twelve hours or longer and the cervix did not dilate. Most of these patients were certainly never in labour, else how is it that in the past ten years at the University Hospital in Iowa City it has not been found necessary to do a single Cæsarean section for this indication?

Often after the cervix becomes partially dilated the pains become ineffectual and further dilatation temporarily ceases as does also further progress. In these cases, also, the attendant often resorts to Cæsarean section giving uterine inertia and rigid cervix as the indication. It is not a good indication, because with proper management of the first stage of labour, the administration of sedatives, and the practice of watchful expectancy practically all of these patients will be delivered from below with much less danger to the mother. The trouble is that the management of such a case requires a great deal of time and patience, courage and skill, and Cæsarean section seems to offer the easiest way out. Some of the best obstetricians have never seen a really rigid cervix except in cases where there has been a previous cervical operation or where a tumour is present. The condition cannot be so common then as to constitute one of the most frequently advanced excuses for Cæsarean section.

Malpresentations and malpositions. — These can be delivered by skilful management from below with a much lower maternal mortality. Breech, brow and transverse presentations *per se* are certainly never indications for Cæsarean section.

Hydrocephalus. — This condition is always treated best by draining off the excessive fluid and delivering the collapsed head from below. The procedure is very simple and requires only a trocar and cannula, or at times just a pair of long scissors. Cæsarean section is never justified although frequently done for this indication. Thus, there were no less than nine Cæsarean sections for cases of hydrocephalus in

the Iowa State investigation. One case was particularly interesting.

> The patient had been in labour for thirty-six hours, with the membranes ruptured and the head floating. The attendant finally decided to do a version and managed to deliver the entire body without difficulty. He was unable, however, to extract the head. After careful thought, he hit upon a plan. He severed the body from the head, and then performed a Cæsarean section to remove the head. He crowned all this bungling by one piece of good judgment. He removed the uterus as well, otherwise the patient would almost certainly have died of infection. As it was she fortunately survived, but at what a cost and at what a risk! All this could have been avoided if he had resorted to the simple expedient of puncturing the head and draining off the fluid, whereupon the delivery could be completed from below with very little difficulty and practically no danger.

These cases of hydrocephalus and many other congenital anomalies could be recognized and treated properly if the very wise practice of always getting an x-ray before resorting to operation were strictly followed.

Previous Cæsarean sections.—When the previous pregnancy has been terminated by a Cæsarean section which was known to have been uncomplicated by a febrile post-operative course, particularly if it was a low section and if there is no other good reason for performing a Cæsarean in this pregnancy, the patient may be allowed to deliver from below. It is very important to be on the watch for rupture of the uterus and to have all in readiness for operation, without delay, should this complication arise. In all cases where there is the least doubt as to the strength of the uterine scar, it is best to do an elective section at term.

Repeated unexplained stillbirths. — This is sometimes offered as an excuse for doing a Cæsarean section before term. The fact that a woman has lost two or three, or even five, successive babies does not indicate that she will lose the next one, as anyone with experience knows. Moreover, the same result can be obtained by induction of labour with rupture of membranes and bagging, if necessary, with much less danger to the mother. It should be stressed, that with very rare exception, the safety of the mother is always to be considered before that of the child.

There are many other reasons that lead men to perform Cæsarean sections that cannot be considered indications.

(1) Cæsarean section offers an easy way out of all obstetrical difficulties. It requires very little art and is an excellent substitute for experience and judgment. (2) It is the shortest way out. It saves the attendant a great deal of time, work and worry. (3) It is much more dramatic and likely to make a good impression on the family. One gets very little credit for a skilful, successful delivery from below, but even an unnecessary Cæsarean section usually makes the family feel that the attendant has done something wonderful and has saved the mother's or the baby's life. (4) It is often done against the attendant's own better judgment, because the family is getting anxious, and he is afraid that they will call in someone else who will advise operation and take all the glory. (5) One can demand a much larger fee for a Cæsarean section than for a vaginal delivery. (6) Some patients demand the operation in the mistaken notion that it will prevent them from having any pain or suffering.

Obviously all of these excuses cannot be justified, but we see them influencing the judgment of our surgeons and obstetricians all the time.

CONCLUSIONS

Cæsarean section is often done without sufficient indication. Most Cæsarean sections today are unnecessary. The chief reason for this is that the attendant has not had sufficient experience in handling difficult obstetrical cases, and consequently fears the outcome. Because of this it is essential always to consult with an expert, conservative obstetrician before deciding on operation. The decision should, as a rule, not be left to a surgeon but to a man who is doing a great deal of conservative obstetrics, every day. Any surgeon can perform the operation, but only an extremely capable and experienced man can tell when it is necessary and even he will sometimes make mistakes.

It is a great pity that so many men are preaching Cæsarean section and developing in the medical profession a false sense of security, when most of the leading obstetricians are convinced that far too many Cæsarean sections are being done already. Each case must be considered from all aspects before resorting to so dangerous an operation.

SUMMARY

1. Cæsarean section has a definite useful place in obstetrical practice, but it is being done far too often for inadequate indications.

2. Cæsarean section, even in the best hands, has an inherently high morbidity and mortality, and should be replaced as much as possible by skilful conservative vaginal deliveries.

3. In the absence of absolute indications for Cæsarean section, the opinion of a well trained obstetrician, widely experienced in conservative methods, should always be sought before subjecting the patient to operation.

4. Most obstetrical complications, including disproportion, hæmorrhage, toxæmias, and heart disease can usually be treated conservatively with a far better outlook for the mother than by Cæsarean section.

5. The life of the mother should never be unnecessarily jeopardized to save the unborn child.

6. The medical complications of pregnancy do not in themselves constitute an indication for Cæsarean section.

7. Lack of time, lack of courage, lack of skill, and lack of judgment are not valid indications for Cæsarean section.

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ESSENTIAL UNSATURATED FATTY ACIDS IN THE RELIEF OF THE COMMON COLD

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THERE has evolved in the literature the concept of a new substance, termed "vitamin F", which is apparently essential for the well-being of animals and man. This substance is associated with and may be identical with an unsaturated fatty acid, linoleic acid. When it is referred to as vitamin F it should not be confused with the term vitamin F which was formerly applied by some American authors to vitamin B_1, an old use of the term which is now discarded. Practically all scientific investigation of vitamin F has been confined to animals, chiefly the rat. Experiments on man have been few and for the most part in the field of pædiatrics. The demonstration of its possible therapeutic use in the field of skin diseases[4, 6, 8] has led to the commercial preparation of many soaps and creams incorporating it, for example "Vitamin F Nourishing Cream", "Vitamin F Skin Cream", "Vitamin F Soap", etc.

The syndrome produced by diets deficient in fat in rodents has been described by Burr and associates in a number of papers, for example, that given in reference 4. Animals fail to grow or to reproduce normally. Their skin becomes dry with many sores, the hair is scanty and dandruff is profuse. Renal degeneration eventually sets in and blood may be found in the urine. The animals consume huge quantities of water, suggesting that the pituitary gland may be involved. Part or all of these findings have been confirmed by others, such as Sinclair[10] and Evans and his associates.[5] None of these symptoms were relieved by administering the fat-soluble vitamins A, D or E,

but they promptly disappeared upon giving fat. By separating the various fat fractions it was eventually found that fatty acids of two or more double bonds (linoleic, linolenic, etc.) were the essential fractions. All types of unsaturated fatty acids are not equally efficient, indicating that the essential one is probably a specific unsaturated fatty acid, and probably a specific isomer. Little has as yet been done on the quantitative bio-assay of this substance but at least one method has been published.[5] In it the unit, provisionally known as the Shepard and Linn unit, is the smallest amount required to prevent the appearance of the first epidermal sign of deficiency, which is usually scaliness, in rats whose diet is deficient in vitamin F. Linseed oil and soya bean oil contain large amounts of the essential unsaturate, while mineral oil and cod liver oil have very little.[8] The substance is effective when rubbed into the skin and is present in a number of official ointment bases, *e.g.*, Sapo Mollis U.S.P. prepared by the old process.

Information on the clinical value of these essential fatty acids is meagre. Hansen[6] reported that in infantile eczema the amount of unsaturated fatty acids in the serum was diminished and that corn oil or linseed oil improved the eczema and raised the serum values to normal. Brown and Hansen[3] later obtained quantitative differences in the serum content of linoleic and arachidonic acids in eczematous subjects. Two years ago one of us (E.M.B.) reported in this *Journal*[2] that a considerable fluctuation took place in the content of unsaturated fatty acids of the serum in patients with fever and infection. At the same time an article by Oncken appeared in the *Illinois Medical Journal*[7] which did not come to our attention until a year later, in which it was shown that the serum unsaturated fatty acids tended to fall in periods just preceding the onset of a common cold. In a small number of experiments, "not sufficiently controlled by exhaustive experiment and study to warrant any sweeping generalizations", Oncken found that feeding oils containing unsaturated fatty acids prevented the onset of colds and elevated the serum unsaturated fatty acids to normal.

In the present investigation a systematic study was made to determine if these unsaturated fatty acids had any real value in the prevention and treatment of the common cold. The preparation used was "Vitamin F" supplied to us in the form of perles containing 3 minims each by the Pharmaceutical Specialties Company of Chicago. Through the courtesy of Mr. K. S. Williams of that firm we have been informed that this substance is a purified, concentrated mixture of linoleic and linolenic acids prepared from refined linseed oil. Fifteen minims (5 perles of 3 minims each) was arbitrarily chosen as the daily dose after preliminary trials indicated that this amount was well tolerated. The daily dose was not varied because we wished to keep the number of variables in our results as few as possible. During the first week of its use a number of the subjects reported nausea and vomiting when the perles were taken on an empty stomach. We therefore advised their use with meals, divided into 2 or 3 daily doses. In the majority of instances the unpleasant reactions did not appear when the perles were so taken. From the data of Brown and Hansen,[3] in conjunction with those given by Boyd,[1] it may be calculated that this daily 15 minim dose corresponded roughly to one-half of the total amount of linoleic and arachidonic acids present in the entire blood plasma of a normal man.

A total of 106 young men, mostly medical students, cooperated in this investigation. They were divided into two groups, those who stated they were susceptible to colds and those who were not. As was to be expected, and as shown in the accompanying table, a few men were inadvertently included in the wrong group. There were 41 men who said that they were subject to many and severe colds each winter, and 65 who noted that they were relatively free of colds. A period of seven weeks, beginning January 1, 1937, was chosen to determine the frequency and duration of colds in each group without treatment with vitamin F. During this initial period, the 41 cold susceptibles (whom we may call Group A) had a total of 63 colds which lasted a total of 454 days. The average number of colds per man in Group A during this time was 1.54 and the average duration of each cold was 11.1 days. At the same time, the group of 65 men who were relatively free of colds (whom we may call Group B) had a total of 53 colds lasting a total of 248 days, or an average of 0.82 colds per man, lasting 3.8 days each.

During a second period of seven weeks, each man of Group A was given 15 minims daily of vitamin F, and no vitamin F was given to the men in Group B who were used as controls. Weekly records were taken of the number of colds and the duration of each in both of the groups. In addition, notes were made of any unpleasant reactions and of any other points of interest.

During the period of treatment with vitamin F the total number of colds of the men in Group A fell to 23, and the average number of colds per man to 0.56. Since in both instances a period of seven weeks was used, it is obvious that there was a decrease of 64 per cent in the number of colds in the cold-susceptible Group A, a decrease which in view of the changes in the control group may be concluded to have been due to the vitamin. In the control Group B at the same time there was less change in the incidence of colds. The total number of colds during the second period of 7 weeks was 41, or a mean of 0.63 colds per man. From January to March, therefore, the number of colds in Group B dropped an average of but 22 per cent. It would appear then that the use of vitamin F resulted in a significant lowering of the incidence of colds. Comparing the mean colds per man during the second period of seven weeks, it appears that the incidence in the cold-susceptible Group A has been lowered to about the same as that in Group B which was relatively free of colds. This would suggest that perhaps the incidence of colds could not be lowered further by the use of vitamin F, and that the few remaining colds were due to other factors. The data also suggest that a considerable part of the population suffer from colds as a result of a deficiency of the essential unsaturated fatty acids in the diet.

The effect of vitamin F upon the duration of colds was even more striking. In the untreated Group B the colds during the second period lasted just as long on the average as they did during the initial period of 7 weeks, *i.e.*, an average of 3.8 days to each cold. On the other hand, in the treated Group A the average duration of each cold fell from 11.1 days in the initial period before treatment to 2.5 days while under vitamin F, a decrease of 78 per cent in the duration of each cold. This, contrasted with no change in the duration in the control group,

TABLE

THE EFFECT OF "VITAMIN F" ON THE INCIDENCE AND DURATION OF COLDS

	Previous period		*Treated period*			*Previous period*		*Treated period*	
Case No.	*No. of colds*	*Days ill*	*No. of colds*	*Days ill*	*Case No.*	*No. of colds*	*Days ill*	*No. of colds*	*Days ill*
CASES RECEIVING "VITAMIN F"									
1	4	16	0	0	23	1	4	1	2
2	2	28	1	9	24	3	12	1	4
3	2	17	0	0	25	0	0	0	0
4	1	5	2	6	26	0	0	1	18
5	1	5	1	3	27	2	8	0	0
6	3	21	2	6	28	0	0	0	0
7	0	0	1	4	29	1	21	2	3
8	3	35	1	7	30	0	0	0	0
9	1	7	0	0	31	0	0	0	0
10	1	18	0	0	32	3	15	0	0
11	1	14	0	0	33	3	18	1	7
12	2	10	2	12	34	3	12	0	0
13	1	3	1	7	35	3	10	0	0
14	2	24	0	0	36	3	12	0	0
15	1	1	0	0	37	0	0	0	0
16	2	17	0	0	38	2	7	2	6
17	2	12	2	4	39	1	7	0	0
18	3	25	0	0	40	1	42	0	0
19	1	14	0	0	41	2	7	1	3
20	0	0	0	0					
21	1	4	0	0	Total	63	454	23	104
22	1	3	1	3	Mean	1.5	11.1	0.56	2.5
CASES NOT RECEIVING "VITAMIN F"									
42	1	4	0	0	76	1	7	0	0
43	1	4	1	10	77	0	0	0	0
44	1	2	0	0	78	1	14	1	7
45	2	7	0	0	79	1	7	0	0
46	1	5	0	0	80	1	6	1	3
47	1	5	0	0	81	1	3	1	7
48	0	0	0	0	82	1	4	1	4
49	0	0	1	4	83	0	0	0	0
50	1	6	1	7	84	2	6	1	12
51	1	6	1	14	85	0	0	1	1
52	0	0	1	3	86	0	0	0	0
53	4	10	1	4	87	1	4	1	12
54	0	0	1	2	88	1	4	0	0
55	1	6	0	0	89	1	3	0	0
56	2	12	1	7	90	0	0	1	2
57	0	0	0	0	91	0	0	0	0
58	0	0	1	20	92	0	0	1	3
59	0	0	0	0	93	1	3	1	4
60	3	12	2	10	94	0	0	0	0
61	1	9	0	0	95	2	7	0	0
62	3	17	1	12	96	0	0	0	0
63	1	3	1	10	97	0	0	1	7
64	0	0	1	10	98	1	2	1	2
65	1	10	1	2	99	2	7	2	7
66	1	10	1	14	100	2	6	3	9
67	0	0	1	7	101	1	3	0	0
68	2	15	1	5	102	0	0	1	3
69	0	0	0	0	103	1	4	0	0
70	0	0	0	0	104	0	0	0	0
71	0	0	0	0	105	1	4	0	0
72	0	0	1	6	106	1	4	3	12
73	0	0	0	0					
74	1	2	0	0	Total	53	248	41	250
75	1	5	1	7	Mean	0.82	3.8	0.63	3.8

presents a definite picture of the effectiveness of the unsaturates.

A comparison of mean values seldom tells the whole and sometimes not the correct story. It does not do so in the present instance. Of the 41 men who were treated 12, or 29 per cent, had no relief whatsoever from attacks of the common cold, attacks which were indistinguishable by all ordinary means from those of the remaining men who did obtain relief. The failure to respond did not appear due to failure of the men to cooperate fully. Being medical students, the men were interested in the experiment and faithfully reported the results upon themselves. Of the remaining 71 per cent the majority obtained complete relief from colds, having no colds at all while under treatment. To summarize, 56 per cent of the entire treated group showed complete relief from colds, 15 per cent showed 50 per cent of better relief, and 29 per cent showed no relief. This "all or none" response was a peculiar characteristic noted on analyzing the results.

A total of 29 of the 106 men thus responded favourably to the use of vitamin F. If it be assumed that none of the men in Group B lacked this vitamin, then it may be calculated that about 27 per cent of the population suffer from a certain number of colds each winter as a result of a deficiency of essential unsaturated fatty acids in the diet.

Fourteen of the 41 men under treatment reported disagreeable reactions. The commonest symptoms were nausea and vomiting, which were not severe and disappeared after a few days use of the drug in most instances. As previously noted, nausea and vomiting were much less frequent when the perles were taken with meals rather than on an empty stomach. Only one man had to discontinue taking the substance because it persistently produced vomiting. Diarrhœa was also a common reaction, but this too disappeared largely with continued use of the drug. One subject was forced to stop taking the perles because of dizziness and light-headedness. Two complained of headache, one of epistaxis, and one of abdominal cramps. Three of the men noted a substantial gain in weight averaging about 10 pounds. An interesting observation, in view of the work on eczema, previously described was that one man with acne reported it greatly improved. Ten of the men in Group A suffered from a chronic nasal catarrh; of these 4 reported it relieved, 3 recorded some improvement, and 3 noticed no change.

SUMMARY

Following a control period of seven weeks, beginning January 1, during which colds were recorded, 15 minims of purified linoleic and linolenic acids ("vitamin F") were given daily to 41 medical students for a further seven weeks, and 65 others served as controls. Vitamin F reduced the average incidence of colds by 64 per cent and the average duration by 78 per cent, there being at the same time little appreciable difference in the incidence and duration of the untreated group. Of the treated group, 71 per cent responded favourably, and 29 per cent showed no relief. Unpleasant reactions occurred in one-third of the treated cases, diarrhœa, nausea and vomiting being the chief side effects, but most of these were temporary and disappeared on taking the substance with, rather than between, meals.

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PERORAL ENDOSCOPY*

(OBSERVATIONS IN TWO HUNDRED CASES OF FOREIGN BODIES)

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GREAT advances have been made in many branches of our profession in the past thirty years, and in none has greater progress been made than in peroral endoscopy. When I recall my four years' residence, some thirty years ago, in a hospital for sick children, I recollect only one case of foreign body, and it was not recognized as such until the child, after several days of observation for an obscure chest condition, during an attack of violent coughing coughed up a shoe button. I mention this only to emphasize the fact that before the days of x-ray and peroral endoscopy many cases of this kind were overlooked which would be recognized and treated successfully today. Very few men outside the large centres do much clinical endoscopy, but, nevertheless, I think that laryngologists should become sufficiently efficient to be able to handle ordinary cases, if we are going to fulfill our full responsibility and render our best service to our communities. Because the subject is so broad and my experience has been limited to examination, diagnosis, and the removal of foreign bodies, I am going to confine myself to my own experience.

Much valuable information may be obtained by a careful and accurate history of the accident. We must remember, however, that a foreign body may be aspirated or swallowed without the patient's knowledge; especially is this true in the case of small children. There are certain very definite signs and symptoms which should make us suspect foreign bodies, and a very careful study of the case should be made. We may also get a very definite history of a foreign body having been swallowed, followed by obstructive symptoms, which, examination will reveal, are instances of cicatrices suddenly producing complete stenosis. The initial symptoms of foreign body aspiration, choking, coughing, and gagging, are very suggestive. If, while holding some foreign substance in the mouth, the patient suddenly has these symptoms of laryngeal spasm, he should be considered a foreign body case until proved otherwise. Cough appears as an initial symptom in an effort to prevent the entrance of the body at the laryngeal orifice, and, later, in more or less paroxysmal efforts to rid the air passages. Still later, it is present from the inflammatory reaction due to the irritating presence of the invader. Dyspnœa is a very frequent symptom. It is usually inspiratory in character, but may be expiratory, or both. It may be due to actual obstruction of the air passages, caused by the presence of the foreign body itself, or because of the bulk of the body, plus the resultant swelling and secretions. Dyspnœa may also be due to large foreign bodies lodged in the œsophagus and by pressure obstructing the trachea. Although all foreign body cases are not emergency cases, still many are, especially where for any reason there is marked dyspnœa calling for immediate relief. Pain is often noted, especially in œsophageal cases, but it is apt to be vaguely localized, and may be due to tissue soreness from violent coughing. Sharp foreign bodies in the œsophagus generally give rise to very localized pain. In considering the type of pain in œsophageal cases, it is well to note that localized irritation, as an abrasion caused by a foreign body passing, will cause marked dysphagia, but rarely is the pain constant.

A careful physical examination of the chest will usually enable you to localize the foreign body in the air passages. Especially is this valuable in cases of negative radiographs. One of the most constant and reliable physical signs of foreign bodies which do not produce any bronchial obstruction is limitation of expansion on the affected side. This peculiar phenomenon was first noted by the late Dr. Thomas McCrae, of Philadelphia. To understand the peculiar findings in these cases of foreign bodies in the air passages, it is necessary to remember that the

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bronchi are not tubes of constant calibre; dilatation during inspiration and contraction of the lumen during expiration occur.

There are three definite types which show practically constant signs in the earlier stages of foreign body invasion. These may be explained in terms of valves. First, the "check-valve obstruction".—In this type of obstruction the result is that more and more air is trapped in the lung, causing an obstructive emphysema. Physically, the affected side of the chest is fuller, but the excursions are markedly limited. Tactile and vocal fremitus are lessened. There is marked hyper-resonance. The breath sounds are markedly diminished. Under the fluoroscope there is hyperaeration of the affected side. The diaphragm is low and does not ascend with expiration. It is necessary to have views taken at the end of inspiration and the end of expiration to demonstrate and diagnose this condition on the film. Almost always, at first glance, one places the trouble on the wrong side of the chest, because of the fact that the hyperaerated lung looks so clear.

The second is "stop-valve obstruction".—This is the result of increase in the obstruction until the air is not allowed to pass either way. The result is that the circulation rapidly absorbs the air from that portion of the tracheobronchial tree which is served by the obstructed air passage and atelectasis is the result. Physically, the affected side of the chest is flattened. There is diminished expansion. Tactile and vocal fremitus are diminished or absent. The percussion note is dull. Under the fluoroscope the affected region is dense. The trachea and mediastinum are drawn over to the affected side, and do not fluctuate with respiration. The diaphragm is drawn high and does not descend with inspiration. Again, films at the end of both inspiration and expiration are necessary to demonstrate this. A few organisms are always present in the tracheobronchial tree. So long as ventilation and drainage are unimpaired, the defensive powers of the lung destroy these bacteria or limit their activity. But in the absence of such ventilation and drainage, as is the case when a complete obstruction is present, the defensive powers of the lung are so diminished that suppuration quickly follows, and that, together with the secretions from the membranes of the lung, causes a condition which has been named "drowned lung". This condition clears up rapidly, once the obstruction in the bronchi is removed. The third type is "by-pass valve obstruction". In this type of obstruction the lumen is simply narrowed; air can pass in both directions, but in diminished amount. If there is little obstruction the findings may be absent, but as the degree increases there is one cardinal finding—"the asthmatoid wheeze", of Dr. Jackson, but it has nothing to do with asthma. This wheeze is usually heard at the open mouth, best during deep breathing, and, unlike the true asthmatic wheeze, rarely at the chest wall.

Roentgen-ray studies should be made in every case. Anterior-posterior and lateral roentgenograms should always be made, as double foreign bodies may be found in a lateral film, which would not be revealed by an anterior-posterior film. The x-ray film very often gives valuable information in solving the mechanical problems which arise in attempting to remove foreign bodies, such as indicating on which side the point of an open safety pin is to be found. In cases of non-opaque foreign bodies in air passages, such as peanuts, beans, etc., much valuable information is obtained as to their shape and location by a thorough x-ray study, keeping in mind the three types of bronchial obstruction. In cases of œsophageal obstruction much valuable information may be obtained by the use of a bismuth-filled capsule, as it will give the location of a non-opaque object, or stricture in the œsophagus. If a flat disc-shaped object located in the cervical region is seen to be lying in the lateral body plane it will be found to be in the œsophagus; if, however, the object is seen to be in the sagittal plane it must be in the trachea.

In adults the most frequent foreign bodies encountered are bones. It has been noted that the great majority of these cases occur in patients who are wearing artificial dentures. The absence of dental sensation, particularly auditory, diminishes the ability of the patient to detect a hard substance in the food, and thus bones slip by that otherwise would have been detected.

The majority of foreign-body accidents are in children. In this series 66 per cent were in children under five years. This series also shows that 24 per cent were of organic or vegetable origin, 13.5 per cent coins, 21.5 per

cent bones, 12.5 per cent pins and nails, and 30 per cent miscellaneous — pieces of wood, glass, tooth pick, rivet, peach stone, head of wheat, and jack stone.

In endoscopic work we must remember that all cases should be considered serious until sufficient time has elapesd after the removal for the elimination of post-operative reaction. In bronchoscopic cases, especially in small children, subglottic œdema is the most common, especially in children under two years of age. This is not always due to the trauma produced by the bronchoscopy, but occurs usually in cases where an inflammatory irritation existed previous to the bronchoscopy; for example, the purulent laryngo-tracheo-bronchitis associated with the aspiration of peanuts or other organic material. When symptoms of laryngeal dyspnœa appear, that is, when supra- and infrasternal indrawing show obstruction, and restlessness shows the lack of sufficient oxygen, do not wait for cyanosis, for it does not come. Only a peculiar ashen colour appears, and that just shortly before the heart stops beating from exhaustion. If the patient is not relieved by putting him in an oxygen tent, a low tracheotomy should be done at once. We should not only be prepared for an emergency tracheotomy in all bronchoscopic cases, by having the standard instruments at hand and sterilized, but we should have the consent of guardians to perform any emergency operation that would become necessary.

In œsophageal cases, especially after the removal of large foreign bodies, we should remember that we are dealing with an inflamed, traumatized membrane, and we should adhere to a basic surgical principle, which is, give the inflamed area, whether it be a joint, a membrane, or any other part, physiological rest. This is especially true in the œsophagus. During the past few years I have made it a rule, after removal of large foreign bodies from the œsophagus, to give the œsophagus as nearly complete physiological rest as possible for forty-eight hours following removal, and longer, if indicated. The method I follow is to give nothing by mouth, supply fluids by hypodermoclysis, and nourishment by rectum, and to give sufficient atropine hypodermically to dry secretions in the mouth and so prevent swallowing as much as possible.

The question of anæsthesia is a greatly debated one among endoscopists. Some claim that no anæsthesia is necessary in children, while others favour ether in children and local in adults. Personally, I prefer to use ether by the open method in children over five years, and in adults 10 per cent novocain, locally. In children under five years an anæsthetic is seldom necessary. I have found it facilitates the examination to have the patient fast at least twelve hours, to have the secretions minimized by proper doses of atropine, and, in adults, to have the patient thoroughly relaxed by proper doses of nembutal, followed by morphine and scopolamine. In bronchoscopic cases, once the bronchoscope is in the trachea, I spray the trachea, especially the lower portion and carina, with 2 per cent butyn.

Although foreign body cases are usually brought in great haste, I have found that very few of them are emergencies. The only real emergency cases I have had are those with foreign bodies in the trachea, where dyspnœa is marked. Having made a diagnosis of a foreign body in the upper air passages or œsophagus, the removal should be attempted as soon as possible after its entrance, as the difficulties increase in proportion to the time they are allowed to remain. We should not, however, begin an endoscopic examination until we have prepared the patient the same as we would for a major operation, for which we expect to give a general anæsthetic.

The position of the patient is very important, especially, when in the prone position. Jackson emphasizes the fact that the head must be held just right, which necessitates a trained assistant. In this method the head and shoulders are pulled over the end of the table and held by the assistant, slightly elevated at first, then lowered. This position is practically the same as the straight position described by Johnson in 1908. In this method, or position, the patient lies on his back on the table, with the back of the head touching the table and the neck slightly flexed. The head being steadied by the assistant, this position has the advantage that it is much more comfortable for the patient, not so tiring to the assistant, the muscles of the neck being relaxed, and the operator does not meet with as great resistance. I use a modification of this position, for which

I am indebted to Dr. Simon Jessberg, of Los Angeles. It is a still further modification of the Johnson position, and permits of the high-low position, and, in addition, does not necessitate a specially trained assistant to hold the head. All that is necessary is an extension on the end of your table which can be placed upright at a right angle to the top of the table, to begin with, then lowered to a right angle below. The patient is placed on the table with the shoulders flat and the neck flexed, the back of the head resting against the vertical portion of the table. As soon as the 'scope enters the larynx or œsophagus the end of the table is lowered as required, to give a direct view of the trachea or œsophagus, the head resting comfortably on the padded table. The assistant watches the shoulders and moves the head to right or left as required. In the case of small children, the patient, securely pinned in a sheet, is placed on an ordinary table. The head is held by an assistant, while the arms and legs are attended to by nurses. The small child speculum is introduced between the incisor teeth, and pushed down behind the epiglottis, which is gently lifted, exposing the upper end of the larynx.

In all cases of dyspnœa in small children, although a very definite history of a foreign body having been aspirated may be given, a careful examination of the pharynx, hypopharynx, and larynx, should be made to exclude inflammatory conditions, and especially laryngeal diphtheria. Just recently, I had three such cases referred to me in one month, but in all of which a diagnosis of laryngeal diphtheria was made from direct smears and cultures from the larynx. Two of these cases gave a definite history of aspiration of a button, and a portion of a peanut.

In presenting this paper, I have omitted all technical points and the numerous mechanical problems that have to be solved in each individual case. I will conclude with a brief review of illustrative cases, which have been selected from a series of 202 consecutive cases as tabulated below.

TABLE I.

BRONCHIAL FOREIGN BODIES

	No. Cases	*Deaths*
Peanuts	32	9
Watermelon seed	8	1
Pop corn	2	
Beans	3	
Carrot	1	
Stone	1	
Lead pencil	1	
Wood	1	
Wheat head	1	1
Mucus plug	9	
Copper cap	1	
Citron seed	1	1
Miscellaneous	7	
	68	12

TABLE II.

TRACHEAL FOREIGN BODIES

	No. Cases	*Deaths*
Pins	3	
Corn	3	
Buttons	3	
Glass spicule	1	
Grass needle	1	
Eggshell and Wood	1	
Eggshell	1	
Nail	3	
Price tag	1	
	17	0

TABLE III.

ŒSOPHAGEAL FOREIGN BODIES

	No. Cases	*Deaths*
Bones	31	
Coins	24	
Safety pins	13	
Nails	6	
Buttons	6	
Toothpicks	2	
Peach stone	1	
Prune stone	1	
Meat bolus	11	
Miscellaneous	22	1
	117	1

CASE 1

G.N., 9 years. Difficulty in breathing, giving a history that six days ago she had swallowed part of a lead pencil. The teacher sent her at once to physician, who told her it would pass naturally. Forty-eight hours later the physician was again called on account of restlessness and fever, and a diagnosis of pneumonia was made, involving the left lung. Forty-eight hours later another physician was called, who said pneumonia was atypical, and an x-ray was taken, when a foreign body was found in the left lung, and the left lung showed increased density. The patient referred to me. I found the child in great distress, relieved by violent coughing attacks in which she would get blue. The nurse who accompanied the child said she feared a fatal termination on two occasions en route. Examination showed limited expansion of the left chest, with dullness on percussion; decreased vocal fremitus; the right chest was resonant and apparently normal. The bronchoscope was passed, and the lead pencil found in left main bronchus. Twenty-four hours later left lung showed marked signs of clearing; forty-eight hours later the lung was entirely filled with air.

CASE 2

B.J.B., 3 years. Heavy breathing coming on suddenly. Six weeks before, the child came into the house from playing, with heavy breathing. He had been under treatment for membranous croup by a local medical man, who did not suspect foreign body. Six

weeks later another doctor was called in consultation. The child was very sick, very apprehensive and very emaciated. Temperature, 104° F.; respiration, 60; pulse, 120. X-ray examination was negative. I quickly exposed the glottis and aspirated as a temporary measure, as the child was too sick for bronchoscopy. The child had a fair night and looked better in the morning. The bronchoscope was passed. At the bifurcation a piece of wood with considerable thick, tenacious secretion was found, and a portion of eggshell in the opening of the left main bronchus. Recovery was uneventful.

CASE 3

W.G., aged 3 years. One week before, while eating peanuts, the child began crying, and this was followed by a severe coughing spell. Since then had had coughing spells and vomiting after eating. Temperature to 102° F., the past twenty-four hours, but less coughing. Right chest — limited expansion; vocal fremitus decreased; dullness on percussion; and a few rough râles. Left side—apparently normal. X-ray—the heart was displaced to the right; the dome of the diaphragm was very high on right, low on the left. Increased density on right. A diagnosis of obstruction of the right main bronchus was made, with atelectasis of right lung and compensatory emphysema of the left. The bronchoscope was introduced and thick, tenacious mucus was found in the right main bronchus, with some débris. No definite foreign body was found. The openings of the upper and lower main stem bronchi were narrowed and the mucosa congested. Twelve hours later, there was slight evidence of dyspnœa. Twelve hours later dyspnœa was more marked. A low tracheotomy was done. Five days later the tube was removed, and the patient made an uneventful recovery.

CASE 4

Mrs. C.C., aged 38, was admitted to St. Joseph's Hospital claiming she had a silver dollar in her throat, and gave the following history. Three months before, during a dispute with her husband, she put a dollar in her mouth, and in trying to get it her husband choked her and the dollar disappeared. She had marked dysphagia, and had gradually lost weight, but was afraid to mention it to her husband. Finally she came to the hospital in very weakened condition. On examination with x-ray the dollar was found in the first portion of the œsophagus. It was removed without difficulty. Considerable ulceration of the lateral walls of the œsophagus was found. Recovery was uneventful.

CASE 5

A.T., aged 9 months. A penny in the throat. Three weeks before, while playing with children, had swallowed a penny. X-ray—double shadow, thought to be due to movement. I passed the œsophagoscope and found the penny embedded in œdematous and ulcerated membrane. In front of the penny was a white substance, which appeared to be exposed cartilage. It was found to be movable, however. I removed a button and a penny, which were superimposed.

CASE 6

F.D., aged 5 years. Six hours before the child had swallowed a seven-pennyweight nail. It had had a choking spell at the time but since had been perfectly comfortable. X-ray showed a nail in the trachea, with the head to the left side. The nail was removed without incident.

CASE 7

G.M., aged 4 years, was playing in the sand near a barn, when he was hit by the barn door, had a sudden choking spell, and became cyanotic. The parents thought the child's head had been injured, and consulted me twelve hours later for head injury and difficult breathing. There was no evidence of head injury, and I found the child apparently normal. Physical examination revealed rough breathing and diminished movement of the right chest. X-rays were taken, and foreign body located in right main bronchus, which turned out to be a stone. It was removed eighteen hours after the accident, and the child made a good recovery.

CASE 8

D.T., aged 30 years. While removing the cap from a bottle of home brew (with his teeth) which was unexpectedly wild, the cap entered his œsophagus. When I saw the patient seven hours later he was in great pain, and marked interstitial emphysema was present. I was unable to get the cooperation of patient with local anæsthesia, so ether was given, but could not get traction on the foreign body, as the forceps would slip off the round shoulder of the cap, and as patient was in a very poor condition I decided that further manipulation was inadvisable, especially on account of interstitial emphysema, as I feared injury to trachea. The patient was put to bed, given nothing by mouth; nutrient enemas, and proctoclyæs were given, and atropine sufficient to keep the mouth dry. After six days, the emphysema was gone, so the œsophagoscope was passed, and I found purulent secretion in the lower portion of the œsophagus. On removal of this, the cap was located near the cardia, and I decided that less damage would be done by pushing it through the cardia. This was done, and a gastrotomy was performed at once, removing the cap. The patient made an uneventful recovery.

CASE 9

T.T., aged 3 years. The history was given that the child had been unable to swallow for a week. Did not complain of pain. An x-ray examination revealed a large ring in the first portion of the œsophagus. Then the father remembered the child playing with the ring, and that he had not seen it for the past week. It was removed by means of the œsophagoscope. Recovery was uneventful.

CASE 10

E.H., aged 3 years, swallowed a safety pin twenty hours previously. He had a coughing spell after swallowing the pin, and made attempts at vomiting for about fifteen minutes. Since, [illegible]d of pain on swallowing. X-ray—heart-sh[illegible] was lodged in the first portion of the œsophagus. [illegible] was removed in two minutes.

CASE 11

M.B., aged 3 years, swallowed a small safety pin six hours before, followed by coughing. When seen by me the child was quite comfortable. X-ray showed an open safety pin in the first portion of the œsophagus, point up and to the right. It was removed. Recovery was uneventful.

CASE 12

O.M., aged 14 years, thirty-six hours before had swallowed a tin whistle, and since, had had difficulty in swallowing. The local physician tried to push the whistle into the stomach under a general anæsthetic without success. X-ray revealed a whistle in the first portion of the œsophagus. It was removed under a local anæsthetic.

CASE 13

L.W., aged 15 years, since swallowing a prune stone twenty-four hours before had been unable to swallow even water. She complained of pain about three inches below the suprasternal notch. On further questioning I found that when she was eighteen months old she had swallowed lye, and following the accident, had had

difficulty in swallowing meat and solid food up to three years ago, but had had no difficulty in swallowing during the past three years. The œsophagoscope was passed and a large piece of meat found near the cardia. This was removed. A stricture with a 2 mm. opening was dilated, a No. 4 being passed, and two days later a No. 8 passed without difficulty.

CASE 14

N.T., aged ten months, had difficulty in breathing for the previous twenty-four hours, following a choking spell while eating an apple. Examination—breathing was laboured and evidence of obstruction in left lung. The bronchoscope was passed, and considerable thick mucus and débris were removed from the left main bronchus. During the next seven days the breathing was rather laboured at times, but the child was happy and in no distress. Temperature, 99° F. On the seventh day the breathing became more laboured, becoming worse suddenly, as the child was *in extremis*. A tracheotomy was done at once, as subglottic œdema was suspected, but with no relief, so the bronchoscope was passed at once and a portion of apple core was found in entrance of the left main bronchus. After removal recovery was uneventful, the child returning home on the eighth day after tracheotomy.

CASE 15

Mrs. S., aged 30 years, with a bone in the bifurcation of the trachea. The family physician was called to see a woman who was choking from having swallowed a piece of pork chop bone. She was seven and one-half months pregnant and in great distress. The glottis was cocainized; a 12 mm. tube was passed, and the bone was found at the bifurcation. I must have made undue pressure, as the patient had a spasmodic cough, and expelled the bone through the tube, breaking the mirror of the instrument.

CASE 16

E.A.S., a male, aged 38 years, while eating peach a few minutes before, suddenly had a choking spell. On reaching for the stone with his fingers it slipped beyond reach. Marked dyspnœa followed, and when he reached the office a few minutes later he was quite cyanotic. The œsophagoscope was passed at once, and a large fresh peach stone removed. It was located just below the cricopharyngeus. There was very little blood on the stone, although the external markings were very sharp. Patient was put to bed, small quantity of warm water given by mouth. Twenty-four hours later his temperaure was 102° F., pulse 84, and there was marked tenderness and swelling of left side of neck, and the patient was raising large quantities of mucus. During the next twelve hours the temperature was 104° F., and the swelling in the neck increased. Traumatic rupture of the œsophagus was feared. Cold applications to neck and rectal feeding were commenced, nothing was given by mouth, and atropine hypodermically. On fifth day, temperature had dropped to normal, and swelling also disappeared. Two days later, the temperature remaining normal, the patient was given water, and his temperature immediately rose to 103° F. The œsophagus was again given physiological rest, and rectal feeding resumed. After three days, the temperature was again normal. After another forty-eight hours, water was given, followed by broths, and the patient made uneventful recovery.

CASE 17

C.L., aged 4 years. The family physician was consulted on July 22nd, at which time the child had mild bronchopneumonia. The patient did not return to the doctor until August 17th, when it came with a history of having had a choking spell two days before. The temperature was 100° F., pulse, 96; and respirations, 30, with physical signs of a bronchitis. As the patient was not improving, having coughing spells similar to whooping cough, with two and three spasms daily, on September 18th an x-ray was taken, and a piece of shingle nail, three-fourths of an inch long was found below the second bifurcation of the left bronchus. For ten days afterward the patient had a temperature ranging from 99 to 102° F., but improved rapidly, and is now in perfect health.

CASE 18

A.T., female, aged 26, while eating walnuts twenty-four hours before, suddenly felt a piece of walnut stick in her throat, and since had been unable to swallow solids, and difficulty in swallowing water. No x-rays were taken. The œsophagoscope was passed, and 20 cm. from the incisor teeth I found a stricture with a 1 mm. opening, the opening located centrally. Bougies were passed gradually dilating to No. 6; four days later No. 8 was passed. On questioning further, I found the patient was living with an uncle, and she did not want him to know that she had attempted suicide five years before by drinking lye.

CASE 19

M.O., aged 31 years, had a persistent, irritating, spasmodic cough, following drinking wine from a broken glass. Twelve hours later the patient was referred to me for bronchoscopic examination, as the physician was unable to control the spasmodic and very distressing cough. X-ray examination was negative. Bronchoscopic examination revealed a small spicule of glass lodged in the mucous membrane at the carina. It was removed, and the distressing uncontrollable cough was relieved at once.

CASE 20

J.S., aged 4 years, while playing, got seed corn in the mouth and suddenly had a choking spell, followed by difficulty in breathing. Doctors Hoyt and Smith, of Glasgow, Montana, were called, and advised taking the child to me at once. About 11 p.m. railroad officials called me, asking me to catch the westbound train, as they feared the child could not reach Minot alive. I met the train midway, but the child was just passing. I did an emergency tracheotomy on the train, but it was of no avail. On examination, I found a kernel of corn lodged at bifurcation, the kernel having swollen slowly until it closed the entire trachea.

"Learn to hear, learn to feel, learn to smell, and know that by practice alone can you become expert. Medicine is learned by the bedside and not in the classroom. Let not your conceptions of the manifestations of disease come from words heard in the lecture room or read from the book. See, and then reason and compare and control. But see first."—*Osler.*

EXPERIMENTAL AND CLINICAL STUDIES ON ADRENAL INSUFFICIENCY*

BY R. A. CLEGHORN, E. W. MCHENRY, G. A. MCVICAR AND D. W. OVEREND

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THE first evidence of the importance of the adrenal glands to life was supplied in 1855 by Thomas Addison in his masterly description of the condition now known as Addison's disease. His report stimulated physiological investigation of the adrenal glands and led to extirpation experiments on animals. Conflicting and inconclusive results were obtained in many of the early experiments. Early death following operation was probably often due to surgical trauma or infection, and continued life in some animals to incomplete removal of adrenal tissue.

The striking pressor properties of the gland, demonstrated by Oliver and Schäfer[1] in 1894, focused attention upon the medulla for some two decades. Eventually, however, evidence accumulated which clearly showed that death followed complete removal of adrenal tissue in all species examined. That it was absence of the cortex rather than of the medulla which was responsible for death was proved by the survival of the animals deprived of the medulla alone, and the death of those in which the cortex only was ablated.[2, 3, 4]

By 1926 many features of the effects of adrenalectomy in animals had been established. The average duration of post-operative survival of the cat and dog was found to be about ten days. Rats and rabbits often survived longer, due to the frequent occurrence of accessory cortical tissue. The outstanding blood changes found in animals dying of adrenal insufficiency were:— a marked rise in non-protein nitrogen; lesser increases of potassium, magnesium, calcium, phosphorus and sulphate; abnormally low values for alkaline reserve, sodium, chlorine and, occasionally, sugar; and a loss of water from the blood.[5] Salt solutions intravenously injected were found to extend the life of adrenalectomized animals.[6, 7, 8]

Proof of the endocrine nature of the gland has been furnished by substitution therapy. Prolongation of the life of adrenalectomized animals by the injection of active extracts of adrenal tissue indicates the presence in such extracts of a hormone or hormones secreted by the tissue. Rogoff and Stewart,[9] in 1927, claimed to have accomplished such prolongation by injecting intravenously saline and glycerol extracts of dogs' adrenals. However, only 6 of their 30 dogs survived well beyond the maximum for the controls. Intravenous epinephrine in comparable amounts was ineffective. In the same year Hartman, McArthur and Hartman[10] reported that the use of a saline extract of beef adrenals extended the post-operative lives of adrenalectomized cats to twenty-one days. They proposed "cortin" as the name of the hormone in such extracts.

Efforts to improve adrenal extracts made little progress in the next few years. In 1930, however, Hartman[11] and his co-workers described an extract which extended the period of survival of adrenalectomized animals, revived animals prostrate from adrenal insufficiency, and was nearly free of epinephrine. An extract having similar qualities was made by Swingle and Pfiffner,[12] 1931, who fractionated alcohol extracts of beef adrenals with organic solvents. Confirmation of the efficacy of extracts prepared according to the method of Swingle and Pfiffner soon appeared.[13, 14] Extracts prepared by this method have proved of great value in the treatment of the crises in Addison's disease and in the elucidation of the changes produced by adrenalectomy and the converse changes which follow the administration of extract.[15, 16, 17, 18]

Objections to the Swingle and Pfiffner procedure of extraction are the complexity and the occurrence of toxic constituents in the extract.[13, 19, 20, 21] The former difficulty at least was overcome by Kutz[22] in 1931, who used a simplified technique, extracting the tissue directly with acetone. Another simple method has been suggested by Grollman and Firor,[23] who, by absorbing the hormone on carbon, claim to have obtained a preparation suitable for oral

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use. The clinical advantages of such a preparation are obvious. Unfortunately, Kutz, Grollman and Firor, and others have employed the rat as an assay animal for testing the potency of their extracts. This method is open to serious objection since a considerable number of reports indicate that rats frequently survive adrenalectomy indefinitely and exhibit normal growth. Consequently, if survival and growth are used as criteria of potency, quantitative assay is impossible, though a crude indication of the presence or absence of the hormone in an extract may be obtained. This subject has recently been dealt with in detail by Cleghorn and his associates.[24]

By any one of several methods it is now possible to prepare active extracts of the adrenal glands, but generally the extracts are expensive both to prepare and to purchase, and a manufactured product has been shown to be both inactive and toxic.[25] Several groups of workers have studied the fractionation of extracts in attempts to isolate the active substance. Among these may be mentioned Kendall,[26] Wintersteiner and Pfiffner,[27] and Reichstein.[28]

Recently, considerable emphasis has been placed on the rôle of certain ions, particularly sodium and potassium, in adrenal insufficiency. The observation of Baumann and Kurland,[29] in 1926, that the blood sodium decreases in adrenal insufficiency was confirmed by Loeb[30] for patients with Addison's disease in 1931. Loeb[31] administered salt to these patients with remarkably beneficial results. This has been confirmed by many other workers and extended experimentally, so that recently Harrop[32] and his co-workers and Allers[33] have claimed to be successful in prolonging the life of adrenalectomized dogs for many months by feeding diets high in sodium without the use of adrenal extracts. Still more recently, the deleterious effect of a high potassium intake in adrenalectomized animals has been shown by Allers, Nilson and Kendall,[34] and by Zwemer and Truzskowski.[35] Wilder[36] and his associates found this to be true also in patients with Addison's disease. Possibly for the same reason, at least in part, thyroxin exerts an untoward effect on adrenalectomized dogs maintained on low doses of extract.[37]

THE PROPERTIES OF ADRENAL CORTICAL EXTRACT

In the collaborative work which has been under way in our laboratories we have been able to develop a process by which a bland, potent extract could be prepared on a large scale. Chemical details of the method will be published elsewhere. The final solution is prepared to contain in each c.c. the material secured from 40 g. of beef adrenal tissue. Before use, 0.1 per cent tricresol and 0.9 per

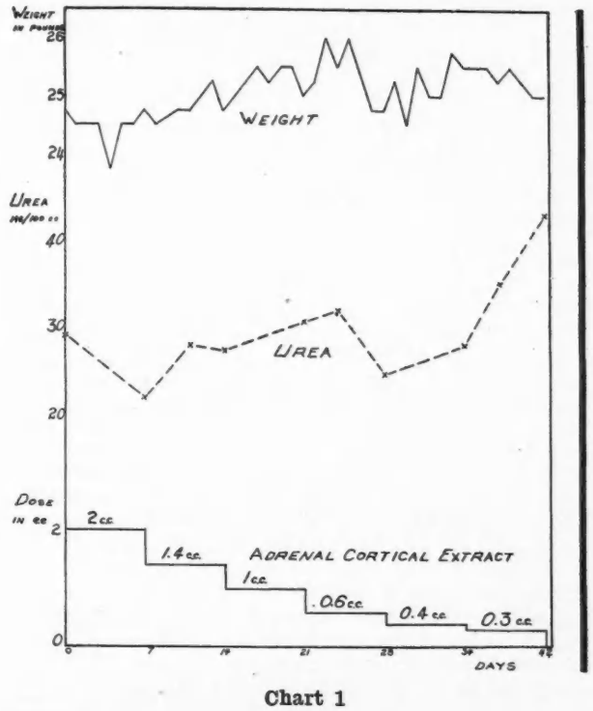

Chart 1

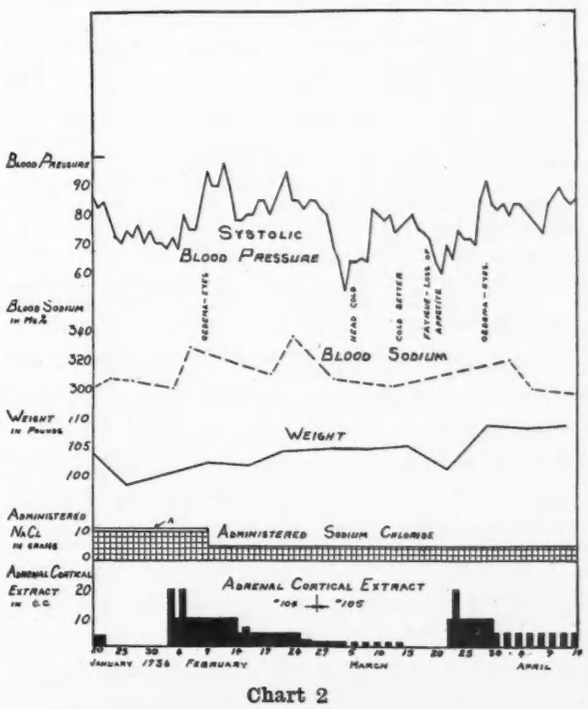

Chart 2

cent sodium chloride are added, and the solution is sterilized by passage through a Seitz filter. The solution is sufficiently free from epinephrine, histamine and choline that 5 c.c. can be given intravenously to an etherized cat without causing any change in blood pressure.

Method of assay.—Reference has been made to the unsuitability of the adrenalectomized rat as a test subject for these extracts. For the standardization of solutions we have employed the completely adrenalectomized dog, and the strength of a solution is expressed in terms of the dog unit as defined by Harrop.[37] This is the minimal amount of extract necessary per day per kilo of dog to prevent an 100 per cent increase in blood urea. Chart 1 illustrates a typical assay.

The procedure of adrenalectomy generally described is in two stages, but it may be performed in a single operation. To aid recovery, glucose-saline and large doses of cortical extract should be given for at least twenty-four hours following the operation. When the dog has completely recovered, it is necessary to demonstrate that all adrenal tissue has been removed. This may conveniently be done by withdrawing extract for three or four days. A marked rise in blood urea indicates that the operation has been successful.

Certain precautions are essential in carrying out the potency assays. The animal must be free of infection and intestinal parasites. The composition of the dog's diet is of prime importance. Since it has been shown that a high intake of sodium and a low intake of potassium are beneficial to adrenalectomized animals it is necessary to ensure a constant level of both elements in the diet. Fluctuations lead to errors in assay. By diminishing the potassium in the diet and increasing the amount of sodium it is possible to secure a high figure for the potency of a given extract. It would be of considerable assistance if various laboratories engaged in the assay of adrenal cortical extracts would use uniform diets. As things stand, potency figures secured in one laboratory cannot be compared with those from another.

The diet in our laboratories consists of an intimate mixture of one-third Purina dog chow and two-thirds fresh, minced, lean beef, plus 2 per cent dried brewers' yeast and 2 per cent Cowgill's salt mixture. Animals are given weighed portions of food. They eat this mixture readily and it maintains them in good condition. In addition to solid food each dog is given 250 c.c. of milk per day. For example, one dog has been kept for twenty months since adrenalectomy and is now five pounds heavier than before the operation.

An improved method of assay is greatly needed. A potency determination on dogs requires at least a month. As has been indicated, the results may readily be influenced by the composition of the diet. A consideration of the variations found in some adrenalectomized dogs illustrates one of the major difficulties of the present method of assay.

Variation in dogs.—As is to be expected in a biological assay considerable differences may be found in the extract requirements of different dogs. For obvious reasons it is impracticable in this work to overcome such a source of error by the use of a large number of experimental animals. It is quite possible, nevertheless, with standardized conditions to compare the activities of different lots of cortical extract by successive assays on the same dogs with a reasonable degree of assurance. Pfiffner[38] and his associates express the opinion that assays done on the same animals are subject to an error of ± 25 per cent, and that assays carried out on different animals may have an error of ± 50 per cent.

The table below illustrates some typical results from our experience.

TABLE I.

Cortical extract	*Dog*	*Weight*	*Insufficient daily dose*	*Estimated sufficient daily dose*	*Estimated potency*
		kg.	c.c.	c.c.	Units per c.c.
No. 106	Brownie	11.3	0.30	0.40	28
	Bonny	10.8	0.60	1.00	11
No. 107	Brownie	11.0	0.25	0.35	31
	Bonny	11.3	0.60	1.00	11
No. 108	Brownie	11.1	0.30	0.35	31
	Bonny	11.0	0.60	1.00	14
	Jerry	11.3	0.60	0.80	11

It can be seen that the three lots of extract show, with any one dog, practically the same potency, although in each case the dog "Brownie" required much less extract than the other dogs.

Extract requirement of cats.—For the assay of extracts, an animal smaller than the dog would offer advantages. The cat would seem to be suitable but for several reasons it is not a convenient test subject for this work. Its susceptibility to upper respiratory infection and the difficulty encountered in drawing blood can with care and experience be largely overcome. However, the amount of extract necessary to maintain the cat in good condition is so much more than that required by the dog that from the standpoint of utilization of extract it is most uneconomical. This species difference in extract

TABLE II.

Extract A106

Cat	*Weight*	*Amount per day*	*Amount per kg. per day*
	kg.	c.c.	c.c.
80 M	5.2	2.0	0.385
82 M	4.6	3.0	0.650
108 M	2.7	1.5	0.550
Diet: NaCl 3.82 g.%; K. 1.45 g.%			
Dog			
Brownie	11.0	0.4	0.036
Pincher	18.0	1.0	0.055
Bonny	11.0	1.0	0.090
Diet: NaCl 2.6 g.%; K. 1.0 - 1.5 g.%			

requirement is not generally appreciated and only careful comparative work revealed the magnitude of the difference in requirement, though the impression gained from use of the cat over a number of years had indicated that a considerable difference probably existed. In Table II the minimal amounts of extract required to maintain three dogs and three cats in good condition are recorded. The sodium chloride and potassium content of each diet is also included for reasons previously emphasized.

USE OF THE EXTRACT IN ADDISON'S DISEASE

During the past two years the adrenal cortical extract prepared by us has been used at the Toronto General Hospital in the treatment of cases of Addison's disease. It has proved of great value in the treatment of patients in crisis, as reported by other workers, and in certain cases, when given over prolonged periods of time, has restored the patients to a measure of health not attained by treatment with salt alone. A detailed account of this work will be published elsewhere.

While we are not prepared to say that all cases of Addison's disease should receive extract in addition to salt during remissions of the disease, the case to be reviewed briefly could not be maintained on salt alone and the patient has benefited remarkably from continuous extract therapy. In view of the fact that the patient was in hospital for a prolonged period it was possible to carry out actual assay of her extract requirement. The salient points in the history are as follows.

The patient, an adult white female, now 26 years of age, was first admitted to the Toronto General Hospital at the age of 16, suffering from typical hyperthyroidism. A small portion of the thyroid gland was removed, and subsequently the patient developed myxœdema, controlled periodically by thyroid extract for a period of 8 years, during which time she had a normal male child in 1930. Some time in January, 1935, she began to vomit once daily and to feel fatigued. Her doctor prescribed thyroid extract in April, and three and one-half weeks later she began to vomit four times daily, to feel dizzy, and became extremely weak. On admission to hospital she presented the characteristic signs of Addison's disease, and was treated with saline and glucose intravenously and with extract intramuscularly. She was discharged from hospital on August 6, 1935, much improved. Sodium chloride, 10 grams daily, was prescribed. Ten days prior to her next admission she contracted a severe head cold and became very weak. She refused to enter hospital, but on December 12, 1935, was sent in in a comatose condition. She showed a very low blood sodium and diminished blood pressure; blood sugar was 0.04 g. per cent. This crisis was treated with saline, glucose and extract intravenously with success, and on December 16th the extract was discontinued. Six days later the patient's temperature rose to 104° F. and she became semi-comatose again. The fever was probably due to cystitis, as pus cells—40 per H.P.F.—were found in a catheter specimen of urine. Vigorous treatment with intravenous saline, glucose and extract again restored her to consciousness. Except for brief periods, she has since received extract without interruption, and the improvement in her condition has been remarkable.

The accompanying chart illustrates her course from January 20, 1936, till her discharge on April 14th. By January 11th the patient's weight had increased to 104 pounds, 11 pounds in excess of her weight on admission. She was receiving 10 grams of sodium chloride and 1 gram of sodium as sodium acetate daily, and felt and ate better, though the blood sodium was still below the normal range. On January 21st the extract, which had been administered in doses of 4 to 6 c.c. daily, was discontinued. The patient's weight and general condition declined rapidly, though she was still receiving the salt by mouth. On February 2nd, intramuscular extract was begun again as the patient was drowsy, darker in colour, weaker, and had vomited. The change within 48 hours was remarkable: the blood pressure and sodium rose, and the weight increased. Œdema became marked; therefore the salt intake was cut in half and the sodium acetate discontinued. The amount of extract administered was reduced every 9 or 10 days till, by March 4, 2 c.c. only were being given on alternate days. About this time the patient developed a slight head cold, the blood pressure and sodium fell and she felt miserable. By March 13th the cold was better, she felt improved, and the blood pressure had returned to about its former level. After four days without extract the blood pressure began to decline and a little later the appetite failed. By the ninth day without extract the patient had lost 4 pounds in weight, felt weak and nauseated, and had a blood pressure of only 60/48. Extract was recommenced and after 9 days' high dosage the weight had increased 7½ pounds, the blood pressure had risen to 92/60, and she felt much stronger. Œdema about the eyes developed but this subsided. The extract was reduced on March 30th to 5 c.c. on alternate days, and she was discharged from hospital on this regimen on which she has continued to date. She now weighs 116 pounds.

It is noticeable that fluctuations in the blood sodium did not closely follow the patient's condition, and that this is more accurately reflected in the blood pressure, body weight, and general sense of well-being. The non-protein nitrogen, such a significant early change in animals, was never higher than 42 mg. per cent during this admission, and was of no use in estimating the patient's condition. This is also true of other cases we have had, though occasionally a high non-protein nitrogen may be seen in crisis.

The adverse effect of even slight infections is most marked in this case, and frequently, in our experience, has accounted for a fatal issue.

The fact that this patient has done remarkably well on 5 c.c. of extract on alternate days does not mean that this is the ideal dose for all cases. Each must be studied separately under constant conditions, and extract should

be given continuously if salt fails to maintain the patient in a reasonable state of health.

SUMMARY

It has been found possible to prepare an extract of the adrenal glands, free from pressor and depressor substances, which may be given intravenously or intramuscularly. This extract has proved useful for the treatment of cases of Addison's disease, particularly during crises. For the assay of this extract, the adrenalectomized dog has been found to be the most useful test animal, and the potency is determined in terms of the amount required to maintain a normal blood urea. Certain precautions should be observed in this assay, particularly with reference to the intake of sodium and potassium; otherwise it is impossible to compare the potencies of adrenal extracts which have been prepared and assayed in different laboratories.

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INSULIN AS A CAUSE OF HIPPUS

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THE occurrence of hippus in the diabetic under treatment with ordinary insulin was somewhat uncommon. Protamine zinc insulin has increased the incidence of this annoying phenomenon.

If the normal pupil be examined under a strong light with a magnifying glass one sees that it is in a continuous state of fine irregular movement, slight dilatations and contractions varying in rhythm and amplitude. In certain pathological conditions clonic contractions of the iris much coarser in range and visible to the naked eye are observed. This is called hippus. Textbooks on diseases of the eye note the presence of this abnormal pupillary unrest in certain diseases of the nervous system, such as multiple sclerosis and some cases of brain tumour. It has been observed most frequently when there is a scotoma in the field of vision with some injury to the macular or axial fibres of the optic nerve. It is common in alcoholics. Since nothing is found in the literature about the occurrence of this affection in the insulin-treated diabetic, and since it is becoming more common under the new form of protamine zinc insulin it seems worth while to call attention to it.

Examination of the pupils of a patient on insulin with hippus under a steady light reveals spasmodic movements. Frequent small contractions of the iris can be observed. More vigorous movements, anywhere from four to sixteen to the minute, have been counted. Irregularity of rhythm and amplitude are

characteristic. When the iris contracts strongly it does so with a jerk.

It was not unusual to find diabetics complaining of failing vision at the time the diagnosis was made. Sometimes repeated refractions had been done without improvement. Promise of relief with satisfactory diet and insulin often failed of fulfillment, and on examination after trial it was found that hippus was present. If reduction of dosage was possible during the course of treatment this condition was alleviated and the sight became normal. Sometimes, apparently, tolerance was acquired and the hippus disappeared. It would appear that patients on large doses were more prone to suffer from this complaint.

Since protamine zinc insulin is replacing the old form larger single doses are common, and in consequence hippus is seen more frequently and is a source of annoyance to the patient. Some indeed find it interfering with their work. A jeweller, for instance, in whom the new regimen promised freedom from noon and evening doses of insulin and the vexation of repeated hypoglycæmia reactions, after two months finds it difficult to carry on his watch repairing. A chartered accountant complains of visual disturbances while at work. Reading is impossible since the focus changes every few seconds. One patient complains that if he shifts his eye from the page it takes several moments before he can find the place again. Heretofore reasonable assurance could be given that the condition would soon disappear. Now patients are complaining that after several months on protamine zinc insulin the distressing complication is persisting.

It is possible that tolerance may be developed and relief obtained, but it will require a longer time than with the regular insulin. Patients have to be assured that refraction will be of no benefit, that the condition, although disquieting, is not necessarily serious, and that relief may come in time either from tolerance or decreased dosage.

A CASE OF SUBACUTE BACTERIAL ENDOCARDITIS WITH BRAIN ABSCESS*

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DUE to the apparently increasing incidence of subacute bacterial endocarditis the more usual manifestations have become so familiar that probably few "classical" cases are overlooked today. It might appear, therefore, that one more case report has nothing to contribute to the better understanding of this condition; but a disease whose manifestations are so protean, and in which there is no one feature which might not also be present in some other condition, ever presents problems and pitfalls in diagnosis which make it always an exercise in clinical acumen. Such was our experience with the following case.

CASE REPORT

F.R., aged 13, was admitted to the Jewish General Hospital, April 22, 1935, with the following story. She was said to have been in good health and attending school until six weeks before admission, when she "caught cold", manifested by weakness and running nose. She appeared to be feverish every evening, but her temperature was not taken. There was no cough. Her appetite became poor, and she was restless during sleep. She remained in bed for 8 days and was then permitted to go back to school, though she still felt weak and continued feverish in the evenings. On March 18th she attended the Herzl Dispensary with these complaints. In addition, it was elicited that in coughing, one week previously, she had spat up some mucus streaked with blood. It was also learned that she had a brother in a sanatorium with open pulmonary tuberculosis. In the examination it was noted that she was pale, that the thyroid was enlarged, and that the heart rate was 120 per minute. The examination was otherwise negative. She was given a tonic and told to return for observation.

She returned to the Dispensary on April 11th, with the additional complaints of burning sensation in the stomach in the evenings, loss of appetite, and constipation. Physical examination did not disclose any new findings. An x-ray of the chest was taken and was reported as showing an azygos lobe on the right, thickened root shadows, and a soft subclavicular infiltration in the right first interspace. She was examined in the pulmonary clinic and again nothing of note was discovered. She was considered as a tuberculosis suspect, and her mother given instructions as to her care and told to bring her back subsequently.

The weakness gradually increased; anorexia and nausea became marked; she vomited once. Unusual drowsiness and greatly increased fatigability was now noted. There had been a loss of 5 lbs. in the six weeks. The day before admission to the Jewish General Hospital she began to complain of frontal headache; she appeared more tired and sleepy than heretofore and complained of aching pain in the left arm and left leg. On going

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to bed that evening she appeared to have higher fever than before. During the night the mother noticed some twitching of the left leg. The following morning, on awakening, the patient could not move her left arm and left leg. There was now no pain. One of us was called (D.L.M.) at this time and sent her into hospital.

Past history.—She had had measles in earlier childhood, and for the past three years had been subject to recurrent attacks of sore throat. Tonsillectomy had been recommended but was not done. No other illnesses.

Family history.—The father had had pulmonary tuberculosis in his youth. As noted previously, a brother, aged 22, was in the sanatorium at the time for open pulmonary tuberculosis. The mother believed that several members of her husband's family were subjects of tuberculosis. There was no history of diabetes mellitus, rheumatic fever, cardiac or renal disease.

Physical examination.—The patient was unusually tall, well-developed; pale, appearing ill but not in any evident distress. The temperature was 101.8° F.; pulse, 135; respirations, 25. There was a left hemiparesis.

There was no sinus tenderness. The pupillary reactions were normal; there was some left internal rectus weakness. The ears were normal; no mastoid tenderness. The nose showed slight excoriation of the mucous membrane. The teeth were in good condition; the tonsils were small but somewhat reddened; there was some post-nasal discharge. There was no lymphadenopathy.

The chest was normal in contour, moved freely with respiration, was resonant to percussion, and the breath sounds were vesicular throughout. No râles were heard.

The pulse rate some time after admission was 100 per minute; regular blood pressure 120/70. There was no cyanosis or clubbing of the fingers. The left cardiac border was 8 cm. to the left of the mid-sternal line. There was no palpable thrill. Aside from the increased rate, the heart sounds were not remarkable. No murmurs were heard.

The abdomen was somewhat scaphoid and moved freely with respiration. The liver and spleen were not palpable.

Neurologically, there were left-sided hemiparesis, with absent tendon reflexes of the left arm, absent abdominals on the left, increased knee- and ankle-jerks, with positive Babinski, Chaddock and Gordon signs. On the evening of admission she developed rigidity of the neck, a bilateral Kernig sign and a positive Brudzinski mass reflex. Lumbar puncture showed a pressure of 54 mm. of water, clear fluid which flowed freely, a positive Pandy test, and a cell count of 36, with a predominance of polymorphonuclears. No organisms were demonstrable.

The urine was negative. The blood showed a moderate secondary anæmia and a white cell count of 8,700. A differential count showed a slight relative increase in polymorphonuclears with a decrease in lymphocytes.

At this time a diagnosis of tuberculoma of the brain with tuberculous meningitis was made with a fair degree of assurance, on account of the findings at the Herzl Dispensary, the family history, the typical prodromal period in which there was loss of weight and strength, evening fever and digestive trouble, followed by the period of actual onset with headache, constipation and vomiting, the characteristic triad of tuberculous meningitis. The neurological consultant concurred in the diagnosis.

Clinical course.—She showed a variable temperature, with evening rises usually between 102 and 104° F. A Mantoux test (1-1,000 dilution) was positive within 12 hours. X-ray of the chest showed increased bronchovascular markings throughout, but no changes indicating active pulmonary disease. The spinal fluid chemistry was as follows—chlorides, 872 mg. per cent; sugar, 72.0 mg. per cent; total proteins, 51.0 mg. per cent. Repeated examinations of the fluid by direct smear and culture failed to reveal any organisms.

In the meantime the patient became more and more irritable, lying curled up in bed, somnolent most of the time, resenting interference, and was fed with difficulty.

The blood and spinal fluid Wassermann tests were negative, but the spinal fluid colloidal gold and colloidal benzoin tests were reported subpositive. On account of this the consulting neurologist suggested trying an arsenical intravenously. This was done, but following the third injection she began to vomit more frequently, and developed an erythematous rash. The injections were therefore discontinued, with gradual subsidence of the vomiting and disappearance of the rash.

The girl was seen during this time by several consultants who examined her thoroughly and did not find cause to disagree with the tentative diagnosis. One of these reported seeing a choroidal tubercle, though the ophthalmologist, on repeated examinations, stated that he did not see any. An electrocardiogram, almost one month after admission, was reported as being normal. A blood culture was ordered, but through an oversight was not taken, and one of the reports recording the failure of organisms to grow from spinal fluid cultures was mistakenly considered to be the report on the blood culture requested.

Since repeated examinations by a number of men during the early weeks of the patient's course had failed to reveal any significant lesions outside of the nervous system, attention became centred on this and on the spinal fluid examinations almost exclusively, until June 4th, when she was seen by a fresh observer. He listened to the heart, and a systolic and a diastolic murmur were plainly audible. He felt the abdomen, and the spleen was easily palpable at the costal margin. At once the case took on a different aspect. The diagnosis of subacute bacterial endocarditis immediately suggested itself. The record was reviewed and the mistake concerning the blood culture was discovered. A blood culture was immediately taken, and in a few days was reported as showing growth of *S. viridans*. This was later repeated, with the same result. The diagnosis was no longer in doubt. Later she developed petechiæ on various parts of the body. Another electrocardiogram, taken July 9th, was reported as showing changes indicative of active myocardial disease. She died on July 10, 1935.

Autopsy.—The significant findings were: a single polypoid vegetation on the aortic leaflet of the mitral valve; vegetative and ulcerative endocarditis of the aortic valve, with aortic stenosis and insufficiency; and an abscess with greenish-yellow pus about 1 cm. in diameter in the region of the right thalamus.

DISCUSSION

We are reporting this case for several reasons. In the first place, the occurrence of a brain abscess in the course of subacute bacterial endocarditis is very unusual. George Blumer[1] in his monograph states that "The striking feature of the embolic manifestations of subacute bacterial endocarditis as contrasted with those occurring in the acute form of the disease, is the lack of suppuration". He notes, however, that out of 35 brains showing evidence of embolism, 2 showed abscesses. Winkleman and Eckel,[2] reviewing a small series of cases of subacute bacterial endocarditis with cerebral complications, all due to the *S. viridans*, found one case with multiple brain abscesses. These authors come to the conclusion that the intracranial

lesions in this disease can be divided into four groups: (*a*) multiple abscesses; (*b*) meningitis; (*c*) embolic lesions with "ischæmic cell disease"; (*d*) toxic endarteritis.

Rabinowitz, Marcus and Weinstein,[3] reporting a case with brain abscess in March, 1932, were able to cite only five other authors who reported a similar occurrence, and stated that Dr. Emanuel Libman, in a personal communication, informed them that he had never observed a case with brain abscess. These authors were impressed by the occurrence of a leucocytosis up to 30,000 and a polynucleosis in their case, and stated: "If, therefore, we were again to encounter a case of subacute bacterial endocarditis with suddenly occurring hemiplegia and a very high leucocytosis and polynucleosis, and if there were no other suppurrative lesion present, we should be very strongly suspicious of the existence of a complicating brain abscess". The white cell count in our case never rose above 12,600. We have not found, in the literature available to us, any other attempt at such a correlation. Blumer, in discussing the hæmatopoietic system in subacute bacterial endocarditis, states: "The leucocytes show great variation in different patients and in different stages of the disease. . . In 40 per cent of the recorded counts 10,000 per c.mm. was not exceeded; in the remaining 60 per cent counts of from 11,000 to 55,000 leucocytes per c.mm. are noted. . . The polymorphonuclear counts range from 26 to 89 per cent. . ".

Another, and perhaps more unusual, feature is the occurrence of an intracranial complication at least several weeks before any discoverable evidence of heart disease. All the reported cases which we were able to trace, with one exception, showed some evidence of cardiac abnormality at the first examination. Among the cases reported by Kimmelstiel[4] was one which was similar to ours in this respect. Ulceration of a valve is uncommon in subacute bacterial endocarditis. Osler[5] notes its rare occurrence, and states that it is the aortic valve which is usually involved. This was the localization in our case.

Finally, we are reporting this case because, for a long time we failed to arrive at the correct diagnosis, and we think that under comparable circumstances others may be similarly misled. The data which militated against our making a correct diagnosis early were: (*a*) the family history of tuberculosis, with recent exposure of the patient to an open case; (*b*) a previous x-ray report of a pulmonary lesion; (*c*) a slowly evolving illness in a young person; (*d*) a sudden onset of a cerebral lesion with hemiplegia and signs of meningitis; (*e*) a positive tuberculin reaction; (*f*) a consultant's report of a choroidal tubercle; (*g*) a clinical course quite compatible with the presumptive diagnosis. Further, there were at first no findings; particularly, were there no cardiac findings or history to suggest any other diagnosis to the various men who examined her.

It is said that multiple arterial embolism is the hallmark of subacute bacterial endocarditis. Our case showed evidence of only a single lesion for a long time before the development of recognizable endocarditis and multiple embolic lesions. Is it possible that the cerebral lesion was the primary focus, and that the endocarditis and embolic manifestations were secondary to it?

The portal of entry was likely the tonsils, but, unfortunately, cultures were not taken from these.

SUMMARY

We report a case of subacute bacterial endocarditis with the following uncommon features: (*a*) the occurrence of an "embolic" manifestation long before recognizable evidence of endocarditis or other of the common clinical features; (*b*) the occurrence of a brain abscess, 1 cm. in diameter in *S. viridans* septicæmia; (*c*) ulceration of a valve in viridans endocarditis.

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LEUKÆMOID BLOOD PICTURE IN TUBERCULOSIS*

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THE present paper records two cases of acute generalized tuberculosis with hæmograms suggesting acute myeloblastic luekæmia. In neither instance was clinical and post-mortem evidence sufficiently definite to prove the coexistence of leukæmia and tuberculosis, though in one case it was suggestive. The cases are therefore presented as examples of a leukæmoid blood picture in tuberculosis.

DISCUSSION OF THE LITERATURE

The coexistence of acute leukæmia and miliary tuberculosis has been reported infrequently. Opinions differ as to whether such cases represent the simultaneous occurrence of two diseases or are really one disease—miliary tuberculosis with a leukæmoid blood picture. Roth[1] was one of the first to record a case of miliary tuberculosis in which the hæmogram suggested acute myelogenous leukæmia though the post-mortem failed to substantiate the blood findings. From the moderately extensive literature three reports have been selected as illustrative of different views on the subject based upon carefully studied cases. The first report is by Wiechmann[2] who recorded the case of a woman of 37 years who died after a short illness of acute miliary tuberculosis and bronchopneumonia. The hæmogram showed 2,260,000 red cells; 40 per cent hgb.; and 35,850 leucocytes, of which 63.5 per cent were myeloblasts and 15 per cent myelocytes. Post-mortem examination showed miliary tuberculosis of all the parenchymatous organs. Definite leukæmic infiltration of these organs was not found. The bone marrow of the femur was very hyperplastic and showed many myeloblasts and myelocytes but no tuberculosis. The author believes that such cases should be regarded as miliary tuberculosis with secondary myeloblastosis and not a true myeloblastic leukæmia.

The alternate view was taken by Lenhartz,[3] who reported the case of a male of 47 years admitted with fever, chills and loss of weight of a month's duration. Examination revealed only enlarged cervical lymph nodes and the following hæmogram: red blood cells 4,060,000; hgb. 74 per cent; white blood cells 8,400; myeloblasts 20 per cent; myelocytes 15 per cent; young polymorphonuclears 34 per cent; polymorphonuclears 20 per cent; monocytes 10 per cent and lymphocytes 16 per cent. As the disease progressed the anæmia became more grave and the leukæmic changes more evident. Shortly before death the hæmogram showed 2,300,000 red blood cells; hgb. 38 per cent; 113,200 white blood cells, of which myeloblasts were 50 per cent and myelocytes 11 per cent.

Post-mortem examination revealed acute miliary tuberculosis of the lungs, cervical and paratracheal lymph nodes. The spleen weighed only 250 grams, and showed no definite evidence of leukæmia, being more "septic" in appearance. However, the liver and some of the lymph nodes showed typical leukæmia infiltration. The bone marrow was practically normal. The author was convinced that both diseases existed, and debates the question of whether the leukæmia or the tuberculosis was primary. In the summary he states that such cases are true leukæmia with tuberculosis and not simply a leukæmia-like blood picture.

A third report by Gottlieb[4] may be taken to illustrate the aleukæmic blood picture, although the author considered the case to be one of aregenerative anæmia. The patient, a child of 14, with acute miliary tuberculosis showed the following hæmogram: red blood cells 1,200,000; hgb. 28 per cent; white blood cells 1,300; platelets 18,000. Differential count: myelocytes 1 per cent, immature polymorphonuclears 10 per cent, segmented forms 20 per cent, lymphocytes 69 per cent. Smears showed marked anisocytosis and polychromatophilia. Normoblasts numbered 1 to 100 white blood cells. The post-mortem revealed a red hyperplastic bone marrow showing many myeloblasts and erythroblasts, but few myelocytes or normocytes.

It is evident that none of the three cases at post-mortem presented unequivocal evidence of

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leukæmia, though clinically the blood picture was such as to suggest that diagnosis. Three different views are expressed, and each may be correct, though the reviewer remains unconvinced that such is the case.

Renewed interest in this problem has been aroused by the recent experimental production of a leukæmoid blood picture in rabbits infected with human or bovine tuberculosis. In this research[5] the infected animals developed multiple tuberculous lesions after inoculation but did not show a leukæmoid blood picture until after tuberculin was given. The maximal leukæmic reaction occurred usually 24 to 72 hours after the administration of the tuberculin and lasted 3 to 7 days. During this time both blood and bone marrow showed all the hyperplastic changes of true leukæmia. The authors believe that a state of tuberculous allergy or sensitivity of the bone marrow exists in such animals, and that the injected tuberculin provokes a reaction in the marrow and blood similar to that which exists in the skin of the majority of tuberculous persons. They suggest a similar explanation in cases of human tuberculosis with a leukæmia-like blood picture—that "endogenous tuberculin-like products may occasionally stimulate the previously sensitized bone marrow to a hyperplastic condition. As a consequence flooding of the peripheral circulation with cells of the granulocytic series ensues".

CASE 1

J.W., aged 27, was admitted to the service of the late Dr. C. P. Howard on April 11, 1936. He complained of fatigue, headache, cough, sputum, anorexia, night sweats, pain in the right chest, loss of weight, and bleeding from the nose and gums.

Family history.—Irrelevant.

Personal history.—He was born in Austria and came to Canada in 1930. He had worked on a farm and latterly as a handy man in a pastry department of a local hotel. He had had frequent chest colds, usually associated with cough and yellowish sputum. For the last three or four years he had had frequent night sweats. His best weight was 160 pounds, four years ago.

History of the present illness.—The patient was in his usual health until five or six years ago, when he developed a cough with yellowish sputum, more productive in the mornings. Occasionally he experienced a sharp "pick" of pain in the right anterior chest. Although he slept well he had frequent night sweats. Nevertheless he carried on with his work in the usual manner. Three months before admission his cough became worse, and he began to have severe afternoon headaches associated with flushing of the face and a sense of warmth. About this time frequent bleeding from the gums occurred, and he felt tired and weak. On April 7th he had a severe epistaxis which was only controlled by an adrenalin pack. Fatigue and malaise forced him to bed and finally to the medical outdoor department, where admission was advised.

Physical examination. — Temperature, 100.4° F.; pulse, 92; respirations, 22. His weight was 135.5 pounds; his development was good but his nutrition poor. There was some myoidema and myotatic irritability. There were a malar flush, pallor of the skin, and some minute petechiæ over the arms, with a large crop appearing after applying the Hess test. There was slight cyanosis of the lips and finger-nail beds, with slight incurvature of the finger nails, but no clubbing. There was some dried blood on the lips, fresh blood on the tongue, and bleeding from the gums of the left upper molar teeth. Crusting was noted in the left nostril as well as old blood. The conjunctivæ were pale, the scleræ clear, and the pupils reacted to light and to accommodation. The cervical, epitrochlear and inguinal glands were palpable, but shotty. There were no abnormalities of the muscles, bones or joints. The chest was moderately well developed, but there was some prominence of the right chest back and front. Expansion was limited. Tactile fremitus and vocal resonance were well transmitted. The percussion note was impaired over both apices and over the right upper lobe, front and back. The breath sounds were vesicular, but over the apices and throughout the right lung moist râles were audible. The pulse was regular, rate 92, of fair volume and tension; the vessel wall was not palpable; blood pressure, 104/50 (right arm). There was a slight capillary pulse in the finger-nail beds. The heart was not enlarged and the sounds were clear except for a soft blowing systolic murmur at the apex. The liver and spleen were not palpable, nor were they enlarged to percussion.

Laboratory data.—Urine: specific gravity, 1.010 to 1.032; albumin 1 to 4 plus; microscopically, a rare red blood cell, pus cell and cast. Blood: red blood cells, 2,600,000; white blood cells, 6,850; hgb. 50 per cent; platelets, 20,000; C.D., 7.9 microns; bleeding time, 5.75 min. (Duke); coagulation time, 12 min. (Lee and White); retraction of the clot was normal; the Hess test was positive. Differential count: polymorphonuclears, 11; lymphocytes, 37; myeloblasts, 40; myelocytes, 7; degenerated cells, 3; basochromic normoblasts, 2; stippled cells, plus. The sputum showed many acid-fast organisms. The stools were benzidine-positive. The blood chemistry was normal, uric acid being 3.5 mg. per 100 c.c. The basal metabolic rate was plus 8 per cent, and a week later, plus 23 per cent. The fundi, when first examined, were clear, but later multiple hæmorrhages developed. X-ray of the chest showed bilateral involvement, and a repeat plate at a later date showed progression with evidence of cavity formation on the right side.

Clinical course.—The case was presented at staff rounds on April 15th as a case of advanced pulmonary tuberculosis, and the possibility of tuberculosis of the bone marrow (accounting for the leukæmic blood picture) considered. In spite of several blood transfusions and expectant and supportative treatment, the course was downhill, with progression of the lung lesions. The patient died on the 37th day after hospitalization.

Post-mortem.—The gross anatomical findings were fibrocaseous and ulcerative tuberculosis of the upper lobes of the lungs, with scattered miliary tubercles throughout, multiple ulcers of the ileum, and enlargement of the tracheal, aortic, abdominal, mesenteric, axillary and inguinal glands. The bone marrow presented a reddish grey appearance, while there were scattered petechial hæmorrhages over the face and arms as well as over the visceral and parietal pericardium.

Microscopic examination revealed bilateral involvement of the lungs with numerous caseous nodules about which there were a zone of giant cells and marked lymphocytic infiltration. There were scattered miliary tubercles throughout. Sections of the liver showed swelling of the liver cells with compression of the

sinusoids. The whole liver appeared unduly cellular, due to the numerous leucocytes in the sinusoids. These cells were mostly large rounded mononuclears with large vesicular nuclei, some of which contained nucleoli and an opaque cytoplasm; a few had indented kidney-shaped nuclei and more abundant cytoplasm. No definite granules could be seen, but some of these cells were distinctly eosinophilic and had the faintest suggestion of granules. Throughout the portal tract there was a marked infiltration with the same type of cell. In the spleen there was a general increase in the pulp, forming a diffuse cellular mass. Lymph follicles stood out distinctly, and nearly all showed central hyalinization; the hyperplastic pulp showed a great preponderance of the large mononuclear cells as seen in the liver. Nucleated red cells were present in moderate numbers. The lymph glands in the above mentioned regions revealed diffuse myeloid infiltration and in many discrete tubercles could be seen. The lymph tissue of the ileum showed a great accumulation of cells similar to those described above; in the centre of these were necrosis and typical tubercles; the overlying mucosa was ulcerated. The bone marrow showed marked myeloid hyperplasia, and after prolonged search no tubercles could be found. Smears were taken at post-mortem and were examined after having been stained by Goodpasture's and Pappenheim's methods. The material was obviously very much *post mortem*, as all the slides were covered with bacteria. The myeloid cells did not take the Goodpasture's stain, although the control slide, prepared with the same stain and technique, reacted normally. The smears stained by the Pappenheim's method showed some myeloid hyperplasia, but no evidence of erythropoiesis. A few red blood cells were present, and they were mature; nucleated red cells were extremely rare. One multi-nucleated giant cell was encountered. The nuclei of half of the myeloid cells indicated normal maturation. The myeloblasts appeared to be relatively scarce.

CASE 2

J.W., aged 59 years, was admitted to the service of Dr. A. H. Gordon on April 9, 1936. He complained of inability to walk any distance on account of cramps in the toes and legs and increasing weakness. Among his other complaints were blurring of vision, increasing pallor, soreness of his nose, hoarseness, anorexia, cough, sputum, vomiting, sore throat, and soreness of the gums.

Family history.—Irrelevant.

Personal history.—He was born in Montreal and had lived there all his life. At the age of 12 he commenced common labour, and at this he had worked all his life. As a child he had had small-pox, and 25 years ago typhoid fever. Apart from this he had enjoyed good health. At the age of 18 he had gonorrhœa.

History of present illness.—In October, 1935, the patient first began to notice that he was failing in strength and not able to carry on with his work. He was also showing an increasing pallor, and his friends noted that he was losing weight. In 1934 his weight was 165 pounds. About 5 months before admission the patient began to have soreness of the gums and had one tooth extracted. Following the extraction he developed an infection of the gum, which persisted. About this time he had dry crusting in his nose, and attended the Ear, Nose and Throat Outdoor. During the five months cough and sputum had been prominent features, but he never had had epistaxis or hæmoptysis. Anorexia and blurred vision have been other features which have characterized his illness. Ten days prior to admission he suddenly developed hoarseness along with some soreness of the throat. For the previous three weeks weakness had prevented him from getting out of bed, and finally he was brought to the medical outdoor, where admission was advised.

Physical examination.—Temperature, 100.2° F.; pulse, 108; respirations, 20; weight, 131 pounds. He appeared ill; the skin had a yellowish tinge; and the mucous membranes were bloodless. There were no petechiæ, but there was a large bruise on the outer aspect of the right knee. The edges of the tongue were smooth; the dorsum was coated and fissured. The teeth were poorly kept, and pyorrhœa and gingivitis were noted. The pupils reacted to light and to accommodation. There were pingueculæ in both eyes. Several shotty glands were palpable in the cervical regions, also in both inguinal regions, but in the axillæ several glands were felt, hard, and about the size of an almond. Examination of the chest revealed impaired percussion note in the right supraclavicular region and axilla and in both intrascapular areas. The breath sounds at the right apex were harsh, but there was no moisture except for some crepitations at the right base. The pulse rate was regular, 108; the vessel walls at both wrists were thickened, nodular and calcified; blood pressure was 90/48; the heart was not enlarged; the sounds were feeble but clear. The liver and spleen were not palpable, nor were they enlarged to percussion.

Laboratory data.—The urine showed a specific gravity of 1.011, a trace of albumin, and a rare red blood and pus cell. Blood studies showed: red blood cells, 1,620,000; white blood cells, 6,510; hgb., 30 per cent; platelets, 24,000. The cell diameter was 8 microns. Differential count: polymorphonuclears, 50; lymphocytes, 21; myeloblasts, 25; myelocytes, 1; degenerated cells, 3; normoblasts, 3. The leucocytes were mainly myeloblasts, and, stained by Goodpasture's peroxydase method, showed 77 per cent oxydase positive and 23 per cent negative. Gastric analysis showed free HCl. Sputum examination revealed only two tubercle bacilli on one occasion, although repeated search was made. The stools were benzidine-positive. The fundi revealed a right retino-choroiditis. The blood chemistry was normal, except for a fasting blood sugar of 0.169 per cent and a uric acid of 4.08 mg. per cent. X-ray of the chest showed infiltration of the parenchyma of the right lung in the upper lobe and enlargement of the right hilar shadow suggesting glandular involvement.

Clinical course.—The patient at first was considered to be a case of pernicious anæmia and liver extract was given, but as investigation developed myeloblastic leukæmia became the common opinion. In spite of blood transfusions and intravenous therapy the patient became irrational, began to expectorate bloody sputum of a mucoid character, and died 9 days after admission.

Post-mortem.—The gross anatomical findings were tuberculosis of the apex of the right lung with considerable fibrosis, generalized enlargement of the superficial and deep glands, generalized arteriosclerosis, and some necrosis and ulceration of the right vocal cord.

Microscopic examination revealed fibrocaseous tuberculosis in the right apex, but at the periphery of the old lesions were many small tubercules. There was also involvement of the left lung. The liver had a well preserved architecture. There was a slight infiltration of the portal tracts with lymphocytes, but there were no accumulations of leucocytes typical of leukæmia. There was nothing characteristic of tuberculosis. The general architecture of the spleen was well preserved, and the follicles were normal in appearance. There was a focal area of necrosis, not typical, but possibly a lesion of acute tuberculosis. The right vocal cord showed generalized œdema and for a considerable area necrosis and ulceration of the surface down to the cartilage. The underlying tissue was infiltrated with polymorphonuclear cells and lymphocytes. The cervical glands showed extensive caseous tuberculosis. The following glands, (*a*) left axillary, (*b*) at the bifurcation of the trachea, (*c*) region of the transverse aorta, (*d*) right and left hilum, (*e*) region of the portal duct, (*f*) region of the left kidney, (*g*) ascending colon, (*h*) upper and lower mesentery, all showed acute caseous tuberculosis. The bone marrow showed a general myeloid

hyperplasia and a large content of red cells. The myeloid cells were particularly hyperplastic and nucleated red cells were numerous. There were no tubercles, in spite of a focal area of necrosis in one of the vertebræ, the significance of which was uncertain, as the post-mortem was done 44 hours after death. Smears of the bone marrow stained by Goodpasture's and Pappenheim's methods were unsatisfactory, as the material was very much *post mortem*. By Pappenheim's method the marrow showed fairly normal normoblastic erythropoiesis but a marked myeloid hyperplasia. The majority of the myeloid cells were of large non-granular type with one or more nucleoli and clear blue cytoplasm, obviously myeloblasts. A small proportion of the myeloid cells were well developed myelocytes of the neutrophilic and eosinophilic varieties. There was not one polymorphonuclear cell per field; in fact only a prolonged search revealed an occasional polymorphonuclear cell approaching maturity.

DISCUSSION

The two cases were strikingly similar in clinical course and in post-mortem findings, as the following summary shows.

TABLE

	Case 1	*Case 2*
1. Duration of acute symptoms	three months	five months
2. Adenopathy	general	general
3. Old tuberculosis of the lungs	present	present
4. Enlargement of the liver	none	none
5. Enlargement of the spleen	none	none
6. Sputum	acid-fast bacilli	acid-fast bacilli
7. Lung signs	bilateral	bilateral
8. *Blood picture.*—Red blood cells	2,600,000	1,620,000
White blood cells	6,850	6,150
Hæmoglobin	50 per cent	30 per cent
Colour-index	0.9	0.9
Platelets	20,000	24,000
Red cell diameter	7.9	8.0 microns
Differential count.—Polymorphonuclears	11	50
Myelocytes	7	1
Myeloblasts	40	25
Lymphocytes	37	21
Macrocytosis	present	present
Normoblasts	present	present
9. *Bone marrow.*—Tuberculosis	none	none
Myeloid hyperplasia	marked	marked
10. Leukæmic infiltration	liver, spleen, lymph nodes	none
11. Miliary tubercles	general	general

From the clinical aspect the outstanding features were the marked degree of pallor, the extremely few blood platelets with resulting hæmorrhagic phenomena, and the great numbers of myeloid cells in the blood smears. The usual differential staining methods were employed to classify the leucocytes. The cells recorded as myeloblasts were large, non-granular, with large oval or round nuclei containing from two to five distinct nucleoli. When stained by Goodpasture peroxydase method a few of these cells were found to contain oxydase-positive granules. The absence of monocytes in both cases was notable.

At post-mortem none of the parenchymatous organs had the usual appearance of leukæmia, and even microscopic sections failed to show leukæmic infiltration in the second case, although in case 1 the liver, spleen and lymph nodes showed microscopic foci of myeloid cells. However, as already stated, this was insufficient to be apparent to the naked eye, and the pathological department have been unwilling to commit themselves to a diagnosis of leukæmia in either instance. The cases are therefore placed on record as chronic tuberculosis with acute miliary dissemination of the disease, associated with a leukæmia-like blood picture suggesting acute myeloblastic leukæmia.

It is not the purpose of this report to uphold dogmatically either the view that myeloblastosis with grave anæmia may occur in miliary tuberculosis or that myeloblastic leukæmia and miliary tuberculosis as two distinct disease entities are not uncommonly associated. Rather are we anxious to emphasize the fact that cases of acute miliary tuberculosis with a blood picture suggesting myeloblastic leukæmia are not infrequently encountered, and further that such cases present diagnostic difficulties even to the pathologist after a histological study of post-mortem material. The recent production of a comparable pathological state in experimental animals, if confirmed, may point towards this correct answer to this engaging problem.

SUMMARY

1. Two cases of acute miliary tuberculosis are reported in which the blood picture was such as to suggest myeloblastic leukæmia.

2. The question of whether two diseases coexist, or whether the blood picture is simply that of a myeloblastosis secondary to acute miliary tuberculosis is discussed.

The authors' thanks are due Dr. A. H. Gordon for permission to report one of the cases.

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STUDY OF AN EPIDEMIC OF RINGWORM OF THE EXTREMITIES IN AN ORPHAN'S HOME*

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Montreal

THE following study was made in a local orphan's Home, and was prompted by the frequency with which one of us (B.U.) was asked to see its inmates for ringworm of the extremities.

Sixty-five children lived in the home, both sexes being equally represented. The ages of the children varied from 4 to 16, of whom 4 were 5 years of age or under; 29 from 6 to 10; 32 from 11 to 16. Six adults were in constant attendance. The children slept in dormitories, 10 or 12 in a room, and, although provided with their own slippers and towels, interchange was the rule. Two shower rooms were provided, one for each of the sexes, the adults using the children's shower rooms. Other than the ordinary soap and water rinse, these rooms received no especial care. During the summer months a country home was provided where hygienic facilities were still less adequate.

In the fall of 1935 active involvement of the extremities of the children became a distinct problem. Clinical examination revealed findings which were similar to those seen in adults. Twenty per cent revealed only the slightest degree of powdery branny desquamation between the toes; 60 per cent showed varying degrees of maceration, many with fissuring. These findings were noted chiefly in the last web of the toes, less frequently in the third interspace, or in both sites. Twenty per cent manifested vesiculation of varying degrees, most of these involving the sides and undersurface of the toes; in a few instances the soles; and in two children the palms as well. Two of the children also had marked hyperidrosis of the soles with a pernio-like appearance of the weight-bearing surfaces. Involvement of the big toe was not particularly noteworthy.

Among the 6 adult attendants were 2 men with severe maceration between the toes, who for several years had used the boys' shower room. It was felt that these two might have been the original source of the infection.

EXPERIMENTAL INVESTIGATION

Scrapings were taken from the involved areas of all the children and later cultured on Sabourand's dextrose medium.

Each of the children received an intradermal injection of the following preparations: (1) 0.1 c.c. of a 1:30 dilution of stock trichophytin from the Lederle Laboratories, Inc., prepared from one strain of *Trichophyton interdigitale;* (2) 0.1 c.c. of the undiluted trichophytin (dermatotrichofitin)[1] specifically prepared from over 300 strains of fungi; (3) 0.1 c.c. of a 1:30 dilution of trichophytin prepared from the fungus cultured from the children themselves, using the technique described by Muskablitt and Director.[2] The first two tests were made at about the time the scrapings were collected; the third, one year later. The reactions to these preparations were of the usual tuberculin type and were read after 48 hours.

The results are submitted in Tables I and II. Analysis of the cultural findings yields the following facts: (1) Positive cultures of

* From the Department of Dermatology, Montreal General Hospital, service of Dr. J. F. Burgess.

TABLE I.

REACTIONS AFTER 48 HOURS TO INTRADERMAL INJECTIONS OF FUNGUS EXTRACTS IN 21 PATIENTS WITH POSITIVE CULTURES*

Age	*Lederle trichophytin 1:30 dilution*	*Dermato-trichofitin undiluted*	*Autogenous trichophytin 1:30 dilution*	*Clinical appearance†*
8	+	+	–	2
9	–	+	–	2
9	+++	+++	+++	1
9	–	+	±	1+
10	–	+	not done	±
10	–	+	–	2+
11	–	–	–	±
11	++	+++	+++	1+
12	–	+	±	1+
12	+	++	+	2–
12	–	–	–	1+
12	–	–	–	2–
12	+	+	+	2
12	+	+	++	1
13	–	–	not done	1+
13	–	–	++	1+
13	+	++	+++	2–
13	+	+	not done	2
13	–	–	–	2+
14	–	–	++	1+
14	–	–	–	±

* In this table and in the accompany table, – indicates a negative reaction; ± an area of slight erythema approximately 0.5 cm. in diameter; + an area of reaction from 0.5 to 1 cm. in diameter; ++ an area of reaction from 1 to 1.5 cm. in diameter; +++ an elevated area of reaction of 2 cm. or more.

† In this table and in the accompanying table, ± indicates barely perceptible scaling; 1–, 1 and 1+, increasing desquamation and finally marked maceration with fissuring; 2– and 2, varying degrees of vesiculation about the toes; 2+, vesiculation of toes associated with palmar dysidrosis.

Trichophyton interdigitale were obtained from 21, or 32 per cent, of the children. These were obtained only from those 8 years of age or over. (2) Positive cultures were found in the presence of very minor clinical signs, although the majority were obtained in cases which showed more severe manifestations of the disease. (3) Fungus was cultured from a perniolike lesion.

Analysis of the findings with trichophytin yields the following facts.

The reactions to dermatotrichofitin, while roughly paralleling those obtained with the Lederle product, were frequently stronger; in three patients the reaction was weaker while in only one instance was a negative reaction obtained in association with a positive one with the Lederle product. In 10 patients, on the contrary, positive reactions were obtained with dermatotrichofitin where negative ones were found with the Lederle product. This is contrary to the experience of Sulzberger *et al.*[3] No positive reactions were observed from the autogenous trichophytin in children under 9 years of age, whereas 5 were obtained with dermatotrichofitin and 3 with the Lederle product. Positive reactions were obtained with the autogenous trichophytin in 34 per cent of the cases; in 32 per cent with the Lederle trichophytin; and in 46 per cent with dermatotrichofitin.

The results with autogenous trichophytin, although hardly comparable with those obtained with the other products because of the time interval, roughly paralleled the previous findings.

With all three products the following facts are noted. The younger the child, the less like-

TABLE II.

CLINICAL APPEARANCE AND REACTIONS AFTER 48 HOURS TO INTRADERMAL INJECTIONS OF FUNGUS EXTRACTS IN 44 PATIENTS WITH NEGATIVE CULTURES

Age	*Lederle trichophytin 1:30 dilution*	*Dermato-trichofitin undiluted*	*Autogenous trichophytin 1:30 dilution*	*Clinical appearance*
4	–	+	–	1+
4	–	–	–	1+
5	++	++++	–	1+
5	–	–	–	±
6	–	–	–	1
6	–	–	–	1
6	–	–	–	–
6	–	–	–	±
7	–	–	not done	±
7	–	–	–	1+
7	–	–	–	2–
8	–	–	–	1+
8	–	–	–	±
8	–	–	not done	1+
8	+	++++	not done	1+
8	–	–	–	1+
8	–	–	not done	±
8	–	–	–	±
9	–	–	not done	1+
9	–	–	–	1+
9	–	–	–	±
9	–	+++	–	±
9	–	–	–	1+
10	–	+	–	1+
10	–	–	++	1+
10	–	+	++	±
10	++	++++	+++	1+
11	+	++	++	1+
11	+	–	–	2
11	–	–	–	±
12	++	+	++	2–
12	–	–	–	1+
13	++	+++	++++	2
13	+	–	±	1+
13	–	–	–	1+
13	–	+	–	1+
13	±	±	++	1
14	+	+	not done	1+
14	+	+	not done	1–
14	–	+	++	1
15	–	–	not done	1+
15	+	++	not done	
15	–	+	not done	
16	±	++++	not done	2–

lihood there is of obtaining a positive reaction to trichophytin. Positive reactions bear no relation to the findings of a positive culture or to the degree of severity of the clinical manifestations.

TREATMENT

The treatment of the affected children was along conventional lines, those requiring active treatment presenting no particular problem. Emphasis was placed rather upon prophylaxis. Boiling of towels and bathmats was insisted upon. In addition, footbaths containing 2 per cent sodium thiosulphate were placed in the shower rooms. Care was taken that the children stepped into these before and after their baths. The children were also required to use a dusting powder between their toes containing 2 per cent salicylic acid, 10 per cent kaolin, 10 per cent boric acid, in a base of powdered talc.

The children were again examined after a lapse of one year. In that interval no evidence of activity was noted.

SUMMARY

Examination of 65 children in an orphan's home revealed clinical evidence of ringworm in all.

Positive cultures of *Trichophyton interdigitale* were obtained from 21, or 32 per cent, of the children.

As a diagnostic measure, trichophytin, irrespective of its source, was valueless. It is of interest to note, however, that the incidence of positive reactions increased with the age of the patient. The young children almost invariably gave a negative reaction, although clinical manifestations may have been severe.

Prophylaxis was successful in stamping out active manifestations of the disease.

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Case Reports

METHÆMOGLOBINÆMIA DUE TO SULPHANILAMIDE THERAPY*

BY E. H. BENSLEY AND J. B. ROSS

Montreal

Paton and Eaton[1] have reported the occurrence of methæmoglobinæmia as a result of treatment with sulphanilamide. This fits in with our experiences with oral administration of the drug. The occurrence of this pigment in the blood does not appear to be related to dosage; it was found with relatively small amounts, as well as with large doses. In one of our cases, for example, (female, age 11 years), methæmoglobinæmia, with marked cyanosis, was found after two doses only of 7.5 grains each, and in another case (male, age 22 years), after three doses only of 15 grains each. Paton and Eaton[1] found that the methæmoglobinæmia and the resultant cyanosis usually disappear within 24 to 48 hours after the drug is discontinued. This is also in accord with our experience.

In most of our cases, the methæmoglobinæmia did not appear to influence the progress of the disease for which sulphanilamide was used. Therefore, as far as is known at present, its occurrence is no contraindication for continuing the drug. However, little is known of *all* of its possible toxic effects. *A priori*, if it causes methæmoglobinæmia, it may be expected to have other and more serious effects. Its chemical structure alone suggests other possibilities, particularly those of benzene and aniline poisoning. Actually there have been reported from its use acute hæmolytic anæmia and agranulocytosis.[2] It is thus obvious that special attention should be paid to those cases in which methæmoglobinæmia develops rapidly after relatively small doses.

Although the methæmoglobinæmia, *per se*, is, as a rule, not harmful, it may be under certain conditions, as the following case illustrates. Findings relevant to the methæmoglobinæmia only are reported, and it is not intended that the data should be interpreted as evidence for or against the efficacy of sulphanilamide in the treatment of infection.

* From the Departments of Metabolism and Medicine of the Montreal General Hospital, Montreal, Canada.

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REPORT OF CASE

M.M., female, aged 22 years, was admitted to the service of Dr. A. H. Gordon on May 16, 1937 with pneumonia due to *S. hæmolyticus*. She was markedly cyanotic. The first dose of sulphanilamide was given at 2 a.m. May 17th (see Table). On May 19th, it was noticed that, although some of the cyanosis disappeared when she was placed in an oxygen tent, it was still much more marked than would be expected from the lesion in the lung. On the following day (May 20th), as there was no change in the condition, the blood was examined spectroscopically and methæmoglobin was found.* The amount was then estimated quantitatively by determining the difference between the total hæmoglobin by Wu's cyanhæmoglobin method[3] and the oxygen capacity by Van Slyke's method.[4, 5]†

It will be noted that, on the first examination (May 20th), there were 2.5 g. of methæmoglobin per 100 c.c. of blood, that is, this abnormal pigment accounted for 22 per cent of the total hæmoglobin. The total amount of hæmoglobin was only 11.6 g. per 100 c.c. Thus the anoxæmia due to the pneumonia was aggravated not only by anæmia but also by the methæmoglobinæmia, since the latter pigment is unable to carry oxygen; the amount of oxygen-carrying hæmoglobin was 9.1 g. only per 100 c.c. The problem was further complicated by our inability to secure a suitable donor for blood transfusion; the patient belonged to Group II (Moss) but by cross agglutination tests with bloods from donors of Groups II and IV, major agglutination occurred in each case.

In view of the favourable results reported by others with sulphanilamide therapy in hæmolytic streptococcic infections, large dosages of this drug appeared to be indicated, providing they did not lead to further reduction of the amount of hæmoglobin capable of carrying oxygen. Daily estimations were therefore made of (*a*) total hæmoglobin, (*b*) oxygen-carrying hæmoglobin and (*c*) methæmoglobin. The combined data are shown in the accompanying table (see page 64).

It will be noted that except for a slight rise on May 21st, the degree of methæmoglobinæmia did not increase. No sulphates were given by mouth since they may favour formation of sulphæmoglobin. The bloods, however, were also examined spectroscopically for the presence of this pigment.* Its appearance is of clinical importance because of the slow rate of removal of this compound; whereas methæmoglobin disappears rapidly—usually within 24 to 48 hours—after discontinuing sulphanilamide, sulphæmoglobin may persist for as long as six weeks.[1] No sulphæmoglobin was found. Since the degree of methæmoglobinæmia did not increase and there was no formation of sulphæmoglobin, the sulphanilamide was given in large doses until the pneumonia appeared to improve clinically. It will be noted that the methæmoglobin disappeared from the blood 48 hours after the drug had been stopped.

The data of May 20th to May 25th inclusive show that, although the degree of methæmoglobinæmia remained fairly constant, the total and oxygen-carrying hæmoglobin contents of the blood decreased steadily. A further attempt was therefore made to obtain a suitable donor for transfusion. A Group II donor, whose blood showed slight major and no minor agglutination with the patient's blood, was eventually found. On May 25th and 26th, 350 and 150 c.c. of this blood were given respectively, with no unfavourable reactions. It will be noted that the effects of these transfusions were (*a*) cessation of further reduction of the oxygen-carrying hæmoglobin content of the blood and (*b*) an unexpected reduction in the degree of methæmoglobinæmia from 2.1 to 0.6 g. per 100 c.c. with no return to the previously existent level. The total hæmoglobin values suggest that the reduction of the degree of methæmoglobinæmia was not due to reconversion into oxygen-carrying hæmoglobin but to destruction.

The data are also of interest in that they indicate the sensitivity of the spectroscopic method for the detection of methæmoglobin in the blood. A very faint absorption band could be seen in the red region of the spectrum with as little as 0.4 g. of methæmoglobin per 100 c.c. of blood. In another case of methæmoglobinæmia, the characteristic band was seen when the blood contained 0.7 g. The sensitivity of spectroscopic examination, it should be noted, depends upon a number of factors, namely (*a*) type of spectroscope; (*b*) source of illumination; (*c*) visual acuity of the observer; (*d*) dilution of the blood, and (*e*) depth of the layer of solution examined. Bloem,[6] with the use of solutions of methæmoglobin viewed through 1 in 5 dilutions of blood and a depth of one inch, found the limit of the spectroscopic method to be about 0.3 g. per 100 c.c.

SUMMARY

1. Attention is drawn to the occurrence of methæmoglobinæmia due to oral administration of sulphanilamide.

2. Reports of acute hæmolytic anæmia and agranulocytosis following the use of sulphanil-

* The methæmoglobin was identified by the following tests:—The blood was laked with the minimum amount of distilled water which permitted a clear view of the red region of the spectrum. In the first examinations, four volumes of water had to be added to one volume of blood. Later, because of reduction of the hæmoglobin content of the blood, three and then two volumes only of water had to be added to one volume of blood. The laked blood was placed in a tube of 11 mm. diameter and examined with a small hand spectroscope against bright daylight. Proof that the band found in the red region of the spectrum was due to methæmoglobin was established by three tests; the band disappeared immediately on the addition to 3 cc. of laked blood of (*a*) one drop of a 1 per cent aqueous solution of potassium cyanide or (*b*) one drop of Stokes' reagent; finally, the position of the band was not affected by saturation of the blood with carbon monoxide. The methæmoglobin was confined to the corpuscles. Repeated spectroscopic analyses of the plasma showed no methæmoglobin.

† Some of the blood pigment which could not carry oxygen may have been a compound, other than methæmoglobin, which could not be recognized by spectroscopic examination. However, the parallelism between the intensity of the absorption band of methæmoglobin and these quantitative estimations suggests that most, if not all, of the abnormal pigment was methæmoglobin.

* There are numerous reports of sulphæmoglobinæmia following administration of sulphanilamide and its related compounds. This literature has been reviewed by Paton and Eaton.[1] As yet, this condition has not been met with in this clinic.

TABLE

SHOWING DOSAGE OF SULPHANILAMIDE AND RESULTS OF SPECTROSCOPIC ANALYSES AND QUANTITATIVE ESTIMATIONS OF TOTAL HÆMOGLOBIN, OXYGEN-CARRYING HÆMOGLOBIN AND METHÆMOGLOBIN OF BLOOD IN CASE OF HÆMOLYTIC STREPTOCOCCIC PNEUMONIA (Hosp. No. 2734/37)

Date	*Hour*	*Type of hæmoglobin gms. per 100 c.c. blood*			*Intensity of absorption band of met-hæmoglobin*	*Dosage of sulphanilamide (given by mouth)*
		Total	*Oxygen-carrying*	*Methæmo-globin*		
May 16	.....	....	....	....	.....	0
May 17	.....	....	....	....	.....	gr. XV q4h omitting one dose
May 18	.....	....	....	....	.....	" "
May 19	.....	....	....	....	.....	gr. XV q4h
May 20	2.00 p.m.	11.6	9.1	2.5	+	"
May 21	10.00 a.m.	11.7	8.8	2.9	+	"
May 22	9.30 a.m.	10.5	8.6	1.9	+	"
May 23	10.00 a.m.	10.2	8.0	2.2	+	"
May 24	10.30 a.m.	9.9	7.4	2.5	+	"
May 25*	8.15 a.m.	9.9	7.8	2.1	+	"
May 26†	8.15 a.m.	8.9	7.8	1.1	faint	"
May 27	8.15 a.m.	8.6	8.0	0.6	very faint	"
May 28	8.45 a.m.	8.5	7.8	0.7	"	"
May 29	8.15 a.m.	8.3	7.4	0.9	"	"
May 30	12.30 p.m.	9.2	8.1	1.1	faint	gr. XV at 4 a.m. and 8 a.m. only
May 31	11.00 a.m.	8.5	7.6	0.9	very faint	gr. XV q4h starting at 12 noon
June 1	.....	....	....	....	.....	gr. XV q4h
June 2	8.15 a.m.	8.0	7.6	0.4	very faint	gr. XV at 4 a.m. and 8 a.m. only
June 3	1.00 p.m.	7.5	7.1	0.4	negative	0
June 4	8.45 a.m.	7.5	7.4	0	"	0

*Blood transfusion (350 c.c.) at 5 p.m.
†Blood transfusion (150 c.c.) and 175 c.c. 10 per cent glucose in normal saline intravenously at 8 p.m.

amide and the close chemical relationship between this drug and benzene and aniline suggest that search for toxic effects more harmful than methæmoglobinæmia should be a routine.

3. A case of pneumonia due to *S. hæmolyticus* and treated with sulphanilamide is cited as an example of a condition in which methæmoglobinæmia may be harmful.

4. The significance of spectroscopic analyses and quantitative estimations of the different forms of hæmoglobin of the blood is briefly discussed.

5. Data are reported which indicate the sensitivity of the spectroscopic method for the detection of methæmoglobin in blood.

The authors wish to express their thanks to Dr. A. H. Gordon, who supervised the treatment of the above mentioned case of pneumonia, and to members of the staff for the permission granted to one of the writers (E.H.B.) to investigate all of the patients in the hospital who have been treated with sulphanilamide.

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A CASE OF APLASTIC ANÆMIA IN A CHILD

BY GILBERT B. PEAT

Saint John, N.B.

On account of the comparative rarity of aplastic anæmia and of the length of time that this particular case has been under observation and treatment it may be worthy of report.

The patient was a girl, born November 5, 1928, of perfectly healthy parents. The labour was normal, almost precipitate, and nothing abnormal was noted at birth or during the post-natal hospital period. She was breast-fed for five months and during this time, from the 6th week, she had attacks of eczema. I also noticed that she gradually developed a somewhat yellowish skin, with cold hands and feet and a bluish tint to the lips and finger nails. Thinking the breast milk might be at fault, I tried her with a caloric modification of pasteurized cows' milk, but this disagreed, so from the 6th to the 7th month I gave lactic acid milk. This also was not tolerated, so from the 7th to the 14th month protein milk was given, with moderately good results. From 14 to 20 months "klim" was used, and from 20 to 24 months whole milk. Then from 24 to 30 months various articles of diet were

added, little by little. Now in all these periods the least variation from the prescribed formula, and any attempt to enlarge the diet by addition of varied foods, were followed by severe gastro-intestinal upsets—chiefly diarrhœa. Milk alone caused severe eczema, and fruit juices of any kind also caused or aggravated it and set up diarrhœa in addition.

When a year old, Dr. Porter, a pædiatrician, examined the child and he noted the food allergies, the beginning anæmia and the palpable liver edge. He warned about possible cœliac disease, but he also was struck as I had been by her size and general good physique.

During 1930 she gradually got a mixed diet of restricted nature, and did remarkably well. In the winter of 1931 I had her given sunlight ray, but in March the yellowish tint of the skin was so noticeable that an electrocardiogram and blood count were made by Dr. Farris, who found Hgb., 40 per cent; red blood cells, 1,890,000; white blood cells, 6,500. The pathological report, soon after, showed marked achromia, micro- and macro- and poikilo-cystosis. The white blood count was 2,300. I thought the case was probably either Addison's or Von Jaksch's anæmia, and put her on liver—Connaught. Shortly after this, in September, 1931, she had an attack of pyrexia and a gastro-intestinal upset, and began to show marked decline. Sending her to Toronto, Dr. Alan Brown had an exhaustive study made of her. Besides the facts before enumerated, he drew attention to the absence of reticulocytes and the slightly increased fragility of the red blood cells. His other findings were practically negative. He considered it aplastic anæmia with depressed marrow activity, and advised repeated small blood transfusions. Her tonsils were removed, and she was given two blood transfusions, and in the three weeks her hgb. went from 35 to 87 per cent, and the red blood cells from 1,400,000 to 3,800,000.

After arrival home she held her own for only a very short time, in spite of receiving liver, iron and hydrochloric acid. She having relatives in Boston, I advised that she be taken to Dr. Minot, and in December, 1931, she was placed by him under Dr. Blackfan, who also had a comprehensive examination made. He found red blood cells, 1,200,000; hgb. 20 per cent; white blood cells, 5,000; platelets, 200,000; no achromia; no variation in the shape of the erythrocytes. Reticulocytes were rare. Fragility normal. Icteric index normal. Bleeding and clotting time normal. No evidence of increased hæmolysis was shown in the urine or stools,

TABLE

Date	*Hæmoglobin*	*Red blood cells*	*Achromia*	*Microcytes*	*Macrocytes*	*Poikilocytosis*	*Reticulocytes*	*Platelets*	*White blood cells*	*Polymorphonuclears*	*Neutrophiles*	*Eosinophiles*	*Basophiles*	*Lymphocytes*	*Monocytes*	*Myelocytes*
28/ 8/31	44%	1,540,000	++			+	0		4,000	32%		10%	0		58%	liver
28/ 9/31	35%	1,400,000							5,800					70%		2 transfusions
17/10/31	87%	3,800,000							5,200					87%		310 c.c.
4/12/31	35%	1,330,000				+			5,600	50%		2%	0		48%	
4/ 8/31	36%	1,880,000	++	+	+	+			2,300	27%		4%	0		69%	
4/12/31	35%	1,330,000				+			5,000	50%		2%	0		48%	iron
16/12/31	20%	1,200,000	0		+	0	+−	200,000	5,000	35%		6%		59%		
28/12/31	48%	2,800,000														300 c.c.
11/ 1/32	53%	2,720,000	++	+	+	+	0		4,400	30%		4%	0		66%	300 c.c.
26/ 1/32	54%	2,560,000	+	+	+	+				44%		2%			54%	
8/ 2/32	50%	2,280,000	−+	+	+	+	0		3,700		34%	2%	0	58%	4%	
15/ 2/32	40%	1,680,000		+	+		0		5,000		31%	4%	1%	61%	3%	
27/ 2/32	35%	1,690,000	+	+	+	+			2,900		14%	3	1%	79	3	
19/ 3/32	32%	1,500,000														
26/ 3/32	50%	2,700,000														transfusion
23/11/32	40%	1,640,000	+			+			3,400		24%	12%	0	64%		
12/12/32	37%	1,550,000	+			+			2,800		32%	2%	0	26%	0	
28/12/33	31%	1,580,000	+			+			3,000		42%	2%	0	52%	4%	
3/ 1/34	24%	1,430,000	+			+			3,500		31%	1%	0	66%	2%	
9/ 1/34	20%	985,000	+			+			3,000		24%	4%	0	70%	2%	
15/10/34	16%															
22/ 1/35	18%	650,000														
7/ 2/35	37%	1,580,000			+	+	0.025%		2,000		20%	14%	0	64%	2%	liver I.M.
9/ 2/35	37%	1,960,000					0.1%		2,200		24%	6%	0	68%	2%	"
11/ 2/35	36%	1,890,000				+	0.3%		2,000		34%	6%	0	56	4	"
16/ 2/35	28%	1,820,000				+	1.0%		2,400		36%	2	0	60	2	"
2/ 3/35	22%	1,370,000	+		+	+	6.0%		3,000		35	2	0	58	5	"
8/ 3/35	16%	1,400,000	+		+		1.0%		2,200		24	16	0	56	4	
15/ 3/35	16%	1,220,000	+		+	+	1.5%		3,000		60	0	0	38	2	
22/ 3/35	16%	1,160,000	+			+	1.0%		3,300		52	6	0	40	2	
1/ 4/35	21	1,020,000	+	+					1,800		36	10	2%	50	2	
13/ 7/35	25	1,310,000	+			+			2,200		13	6	1%	80	0	
24/ 9/35	20	950,000	+			+			1,800		44	0	0	54	2	
2/11/35	16	980,000		+					1,300		30	4	0	64	2	
22/ 1/36	13	780,000	+			+			1,600		18	2	0	78	2	
25/ 2/36	21	1,270,000	+						1,900		23	5	1%	70	1	
28/ 3/36	19	1,210,000	+			+			2,400		42	0	0	54	4	
17/ 6/36	19	930,000	+			+			1,500		48	2	0	36	4	
14/ 7/36	13%	710,000	+						2,000		28%	2%	0	68%	2%	
9/36	25%	1,240,000														
4/11/36	38%	1,870,000	+			+			2,100		24	16	0	60	0	

both being negative. Skin tests to foods were negative. Blood cultures negative. Gastric analysis showed no free hydrochloric acid in the fasting contents and small response to subcutaneous injections of histamine. X-rays of the chest and long bones were normal. It was concluded that she was a case of primary hypoplastic condition of the bone marrow. She was given two transfusions of 300 c.c. apiece, bringing the hgb. from 20 to 48 per cent and the red blood cells from 1,200,000 to 2,800,000.

It was hoped she would improve with liver, iron and hydrochloric acid, but from December, 1931, to March, 1932, the various counts had dropped so that I sent her back. Liver intramuscularly was tried but with no effect, so another transfusion was given. This gave a quick response, but treatment with iron for a week did not improve it, so nucleotide was given. This caused some reticulocytosis and a maintenance of the hgb. and red blood cells as after transfusion. At this time she developed a febrile attack with diarrhœa. After a protracted recovery she returned home, and from then on she received transfusions of citrated blood of from 300 to 400 c.c. These were given on an average of every six weeks. Besides these, I gave her various preparations of liver, iron, yeast, ventriculin and of bone marrow. A laboratory report on the blood was made each time, and sometimes weekly. I relied, however, more on clinical symptoms than the blood findings. Whenever she became depressed, fretful, and tired, and when a very rapid pulsation or rather oscillation showed in the jugular it was a sure indication for transfusion. Sometimes I let her go for as long as eight weeks, but very seldom. Throughout 1933 and 1934 this went on, holding the hgb. at from 20 to 35 per cent, but with never much sign of regeneration of the blood as evidenced by reticulocytosis.

I was most fortunate in being able to keep in touch with Dr. Lewis Diamond, of Boston, by phone and letter, and he, through his association with Dr. Blackfan, Dr. Murphy and Dr. Minot, gave me the advantage of having at my disposal the newest preparations of various remedies such as I have mentioned. I may say the only thing that seemed to give much help was bone marrow, which for two months had my hopes built high, but after that it seemed to lose any effect. Early in 1935 Dr. William Murphy was in town, and saw her, and he advised liver given intramuscularly two and three times a day if possible. I did manage to give it once a day for a month by which time the performance was on the plane of searching someone out in a dug-out to stick a bayonet into him. So I had an armistice. The red blood cells and hgb. went up for some time during this but began to drop after two weeks. The reticulocytes however went from 0.025 up to 6 per cent but these also soon went down. Shortly after this she developed a severe attack of pneumonia with a temperature of 106° F. and a marked dilatation of the heart. It looked rather hopeless, and, talking it over with Dr. Diamond, he said they got good results in the children by daily small transfusions of blood (50 c.c.). As my own experience with transfusions in pneumonia had not led me to any favourable opinion of it, I was rather dubious, but it certainly worked wonderfully well in this case and she rapidly recovered. From then on I kept to the old method of transfusion, 400 to 500 c.c. of blood every six, five, and four weeks, but the last large transfusion on July 7, 1936, with the hgb. at 13 per cent, red blood cells at 710,000, it was followed by so little improvement that I saw there was no chance this way, and determined if I could get donors that I would give 100 c.c. every week. As all the friends of the family were intensely interested I have been able to get twelve donors, and have been able to give 125 c.c. weekly. She has now received her fourteenth such, and the change has been gratifying. It took several weeks to become noticeable, but at her eleventh the hgb. was 30 per cent. It now is 38 per cent. Her general appearance has altered, the lips being pink, and her expression bright. For the past three weeks she has been able to attend school and has done very well at it. She eats exceedingly well, in fact she has for several years eaten very large meals for her age.

A great help has been the way her veins have increased in size with each year. The first transfusions were in the veins at the dorsum of the foot. Then in the jugular. Three years ago I got a small needle in the arm with a good deal of trouble and it took two hours to give 400 c.c. but now we can get a 19 needle in either arm, and Dr. Gordon Corbet and myself give 125 c.c. at her home every Monday in a very short time. Should improvement keep up and should she get to 50 per cent hgb. I shall give the transfusion every two weeks and so on, as it seems hardly feasible to give weekly transfusions for more than six or eight months. She is also getting a preparation of liver, iron and bone marrow by mouth.

Incidentally the bone marrow findings, done twice in Boston, were as follows.

September 20, 1933.

Sternum.—Three sections with Giemsa stain showed small bits of negative periosteum, perichondrium, cartilage and trabecular bone. In the spaces between the latter there was a small amount of marrow which was interrupted by numerous large vacuoles. Such marrow as remained was apparently active in both erythropoietic and myelopoietic elements. There were unusually large numbers of eosinophilic myelocytes.

April 29, 1936.

Tibia. — Ten sections. Multiple bone fragments presented no abnormal features of structure or appearance. In the bone marrow spaces there were diminished numbers of scattered areas of cell activity. In most areas the marrow space was occupied by fat cells or loose connective tissue. In the scattered areas of activity the cells appeared to be of the myeloid type, with no evidence of hæmatopoietic cells or their activity. There was no inflammatory change. I append a table of the blood findings throughout the course.

I wish to record the names of the medical gentlemen who have made it possible for me to have such comprehensive and authoritative information on every phase of the case, and have helped me as much by their courtesy and consideration as by their scientific acumen, whether as pædiatricians, cardiologists or pathologists, Drs. George Minot, William Murphy, Alan Brown, Donald Porter, Hugh Farris, Kenneth D. Blackfan, Louis Diamond, Harry Abramson, Robert McKean, Gordon Corbet and S. W. Nickerson.

I may further add that these same qualities have elicited for them all such a regard and gratitude from a very winsome little patient and her parents as they can hardly realize.

DUPLICATION OF THE URINARY TRACT

BY J. P. BONFIELD

Ottawa

Pain occurring in the right lower quadrant in human beings has always been one of the most interesting subjects from a surgical standpoint. Many surgeons are so accustomed to view all pains in the right side as indicative of appendicitis that a number of other very interesting pathological conditions are missed.

In this particular case, a young female, aged 21 years, somewhat below par mentally, was admitted to

the hospital with a tentative diagnosis of acute appendicitis. Her leukocyte count was 21,000; her temperature was 103° F.; pain and tenderness were fairly well marked on the right side over McBurney's point and down into the pelvis; and a catheterized specimen of her urine was full of pus cells. In spite of other proofs of acute inflammation there were a number of shadows in the picture that prevented a diagnosis of acute appendicitis.

A diagnosis of acute pyelonephritis was made, with probably a secondary ureteritis, which, in turn, might have involved the appendix, if it were lying in the pelvic position. A conservative attitude was assumed towards the case, and, in one week's time, the acute symptoms had subsided, temperature and leukocytosis disappearing. But pus continued in the urine, pain in the right side persisted, a proper urological examination was refused, and the patient was becoming very dissatisfied. A thickened mass was felt through the rectum on the right side, and it was decided to open the abdomen. A long, subacutely inflamed appendix, densely adherent along the course of the right ureter, was removed with some difficulty. A greatly thickened tube, which was taken to be the right ureter, suggested an advanced inflammatory condition of the genito-urinary tract, which had, as we suspected in the first place, involved the appendix.

The patient did not complain of any further pain in the right side, and she was discharged from the hospital about ten days later, with instructions to report back at the end of a month for further examination. On her return she was far more cooperative and anxious to do exactly as she was told. She was turned over to the urological department for examination and report. The superior right kidney showed calyces dilated 3 X.; hydro-ureter to the bladder, with huge fusiform dilatation of the pelvic ureter. The inferior right kidney showed calyces dilated X., dumb-bell in shape, but the ureter was normal in size. A complete diagnosis showed that the patient had complete duplication of the urinary tract as regards the kidneys and ureters. There was pyelonephritis due to *B. coli* of both right kidneys, with ureteritis and hydronephrosis of the superior right kidney and hydro-ureter. The left side was normal. Both kidneys on this side were negative for infection.

The further surgical treatment suggested to the patient was the removal of the superior right kidney, along with the hydro-ureter. This treatment was refused for the time being, but, no doubt, she will be compelled to have some radical measure done some time later.

A CASE OF OCULAR MYIASIS

BY ROY MUSTARD

Vancouver

Mrs. W., aged 34 years, was first seen on August 1, 1936. She affirmed that the right eye had been itching considerably during the previous week. The previous day she noticed maggots in the eye and succeeded in removing nine live ones by means of a cotton-covered sliver of wood. Since then, however, the itching had persisted, and she was sure more were present.

The right eye was examined with an x 9 lens. Nothing of note was found until the upper lid was everted, when a small, actively-moving grub, slightly less than 1 mm. in length, was seen in the superior fornix. For the greater part of its length it was white in colour, and barely visible, but one end was dark, almost black, in shade. The end containing the dark-coloured substance was slightly broader than the remaining portion.

Removal of the maggot was effected by means of a cotton-covered probe. The dark-coloured portion was lifted from the conjunctiva with difficulty, the remaining portion of the grub, however, was non-adherent. The larva, for such it appeared to be, was placed in normal saline solution, and a search for further specimens was made. Examination of the right eye and then the left failed to show the presence of any further organisms.

A prescription for equal parts of metaphen soluble 2,500 and water was given, to be used as eye drops three times a day. Albolene was also prescribed, to be used thrice daily as eye drops.

The patient was seen again on August 7th. In the interval four dead grubs, she stated, had been removed, but no live ones, though her eyes continued to water and itch to a less degree. Examination of the eyes with an x 9 lens revealed no more larvæ.

No larva was available for microscopic examination, but its characteristics and size as seen under the nine power lens, the time of the year, and the number which had been found, would indicate that this was a case of conjunctival myiasis due to the sheep gadfly (*Œstrus ovis*).

A careful check of the preceding few weeks has failed to produce any enlightening facts except that the patient had been looking after a horse she owned, and had entered it in various races in British Columbia and Alberta. The fact that at some towns the stables were in close proximity to sheep folds was not considered unimportant.

C. P. Schenck[1] states that infection of the eye with maggots is much less frequent than of the nose. In eight ophthalmic textbooks no reference was made to ocular myiasis, and it is merely mentioned in two others. De Schweinitz dismisses it in one sentence as a cause of conjunctivitis.

In 1923 Stark reported a case of sheepbot larva in the eye. He said: "I would hesitate to report a single case, did it not seem to have an exclusive place in the American literature evidenced by the fact that I have found none reported". The larvæ reach 1 mm. in length, have an elongated oval body, broad in front and gradually attenuated in the rear. The mouth hooks are dark coloured, resemble horns, and serve as attachment to the mucous membrane.

The insects may deposit the eggs in the conjunctival sac. Some are viviparous and deposit the living larvæ on the conjunctiva, where they at once begin moving about.

W. M. Lyon, Jr.,[2] says "One source of infection is by the sheep gadfly, and is caused by its depositing living larvæ in the conjunctival sac. The minute larvæ are deposited, as the fly strikes the eye (in a second or less). In the sheep they are deposited in the nostrils and probably at times in the eye. When animals other than sheep are attacked, *e.g.*, man or dogs, the larvæ cause mechanical irritation which may

last up to ten days, after which the larvæ apparently die for want of suitable soil.

"The first stage larvæ, scarcely a millimetre in length, are deposited by the viviparous females in summer or autumn in lots of five to fifty in the nostrils, and no doubt in the eyes, of the sheep. From these places they make their way into the frontal sinuses, and during the winter develop into maggots of considerable size, twenty to thirty millimetres in length. In the spring and summer the larvæ emerge from the nose, fall to the ground, in which they burrow, and there pupate from twenty-five to thirty days, when the adult fly hatches out. These mate, and the pregnant females again infect the sheep. The accident of these larvæ getting into the human eyes appears fairly common in Algeria and Russia, less often in Europe, and rare in the U.S.A. Three cases have been reported in the U.S.A.

"Treatment.—Remove the larvæ on a small cotton-wrapped probe under magnification of ten diameters. It is probable that in the course of a few days the larvæ would spontaneously work out of the eye or crawl down the tear duct, as man being an unsuitable host they would eventually die.

"They are whitish in colour and barely visible in the conjunctiva except for the anterior third, which is distinguished by the dark brown chitinous hooks and accessory apparatus. The discomfort in the eye is caused by the larva inserting its hooks in the conjunctiva, dragging itself forward and repeating the procedure."

No history of penetration of the eyeball or other damage is recorded.

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Clinical and Laboratory Notes

A NEW FOOT SUPPORT FOR TOE AMPUTATION CASES

BY JOS. H. GROVE

Paisley, Ont.

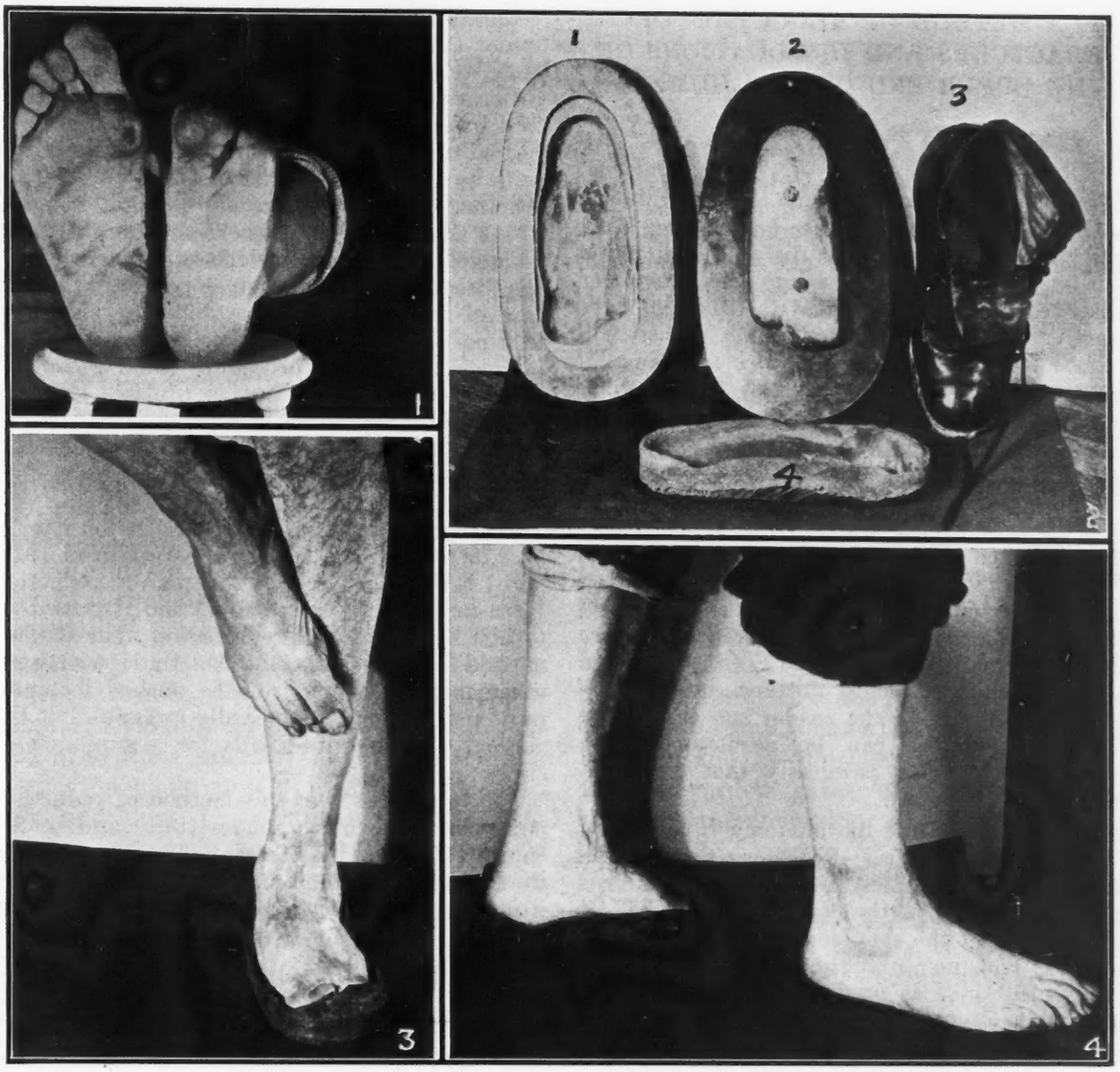
It is obvious that the removal of the great toe, and to a lesser extent the other toes, causes a great impairment of the patient's ability to walk easily and naturally. If the heads of any of the metatarsals are removed as well the disability is increased, on account of the destruction of the anterior transverse arch of the foot.

Boots and arch supports designed to correct these disabilities have been unsatisfactory on account of their lack of flexibility, and because walking has been painful, especially when the transverse arch of the foot is broken and the body weight is borne by the heads of the remaining metatarsals. The design and method of manufacture of a sponge rubber support, which solves the above problems satisfactorily is here described.

The patient, J.McK., lost all his toes and the heads of the three mesial metatarsals of his left foot in 1932. Different boots and supports were supplied by appliance makers in an effort to supply him with a painless and efficient means of walking. None were satisfactory. He could not rise up on the toe of his boot when walking, due to the lack of a support that was both firm and flexible. The heads of his two remaining metatarsals (1st and 5th) carried the body weight when his weight came to rest on the front of the foot in walking, and hence they were always sore, and walking was painful. He could not walk more than a few hundred yards at a time, and this handicapped him tremendously in his business of contractor and bridge builder. Fig. 1 shows the present condition of his feet.

I suggested that if a support could be made that would cushion the foot and have depressions to fit the heads of the remaining metatarsals to equalize the weight bearing, then he would have more comfort. The patient is a natural mechanic, and he set about the problem in his own way. After experimenting with leather, felt, and metal and finding them unsuitable, he thought of rubber, and found it was the proper medium to employ.

A heavy cast-iron die-box, weighing 30 lbs. was made (Fig. 2–1), length 11½ inches, width 6 inches, thickness of walls 1½ inches, height 2½ inches, inside depth 1½ inches, and shaped roughly oval. A steel template, ⅛ inch thick, was made to fit as a lid (Fig. 2–2). An impression of the foot was made in a box of sand, and into this was poured molten babbit metal. The die thus formed was attached to the template by screws. In a rubber factory the die-box was filled with sponge rubber latex, the template with die attached was pressed into the rubber by a hydraulic press, and the rubber vulcanized. Fig. 2–4, shows the support when vulcanized. It is later trimmed with a razor to fit the boot.



The essential points of this support are first the thickness in front, to take the place of the toes in the boot (and note that this is a flexible support); second, the moulded support under the foot, of varying thickness, to conform with the shape of the foot. This part of the support holds up the antero-postero longitudinal arch, and, more important, it supplies a support for the deficient anterior transverse arch. Fig. 2 shows, in addition, the support placed in the boot, and also in the foreground a side view of the support. Fig. 3 shows the patient balanced on the deformed foot. Fig. 4 shows the patient with the support on his foot (without boot), about to place his weight on the anterior part of the support as in walking. The whole apparatus, exclusive of the time employed and the mileage covered, cost twelve dollars; extra rubber supports cost 50 cents each.

An important point in the manufacture is to be sure to have the die-box, template, and die heavy enough, as otherwise the hydraulic press used by the rubber company will be too powerful and will squash the whole apparatus.

The patient has been using this support more than six months, and he can do his everyday work without much handicap. He can walk as far as he wants to without fatigue or pain or limp. The support weighs only a few ounces and needs no special boot. Woollen socks should be worn. The support is not hot on the foot in summer as the rubber contains so many air cells.

The patient was a Workmen's Compensation case, and after he had worn the support for some time he went to Toronto and demonstrated his support to Prof. W. E. Gallie, chief surgeon to the Ontario Workmen's Compensation Board, who was much interested and approves of the principle.

A METHOD OF REDUCTION OF FRACTURES AND DISLOCATIONS OF THE UPPER END OF THE HUMERUS

BY R. S. MURRAY

Stratford, Ont.

One may or may not have had or seen difficulty in the reduction of a dislocated shoulder, but by the time a large enough series has been observed both difficulty and facility will have been encountered. The following method will reduce the troublesome cases to a minimum, if not to zero.

Taking for granted that a proper diagnosis has been made, with or without x-ray, and without anæsthesia, have the patient seated on the floor, tailor-fashion. Standing behind the patient, with a firm grasp of his wrist, abduct the arm until it is fully raised above the head. Then grasping his wrist with both hands, traction is exerted as if in lifting the patient off the floor. The dislocation is now reduced, place the free hand in the axilla and exert an upward pressure while lowering the arm to the side. This may appear to the reader too easy to be true; however, it can be accomplished so quickly and almost painlessly that an anæsthetic is not required.

A consideration of the anatomy involved reveals the fulcrum effect of the acromion process, the withdrawal of the head of the humerus through the rent in the capsule, if such exists, a relaxation of the shoulder group muscles and tendons, and no entangling in tendons commonly mentioned as predisposing factors which prevent easy replacement. Should failure occur without an anæsthetic, such can be administered and similar overhead movements used, with the patient in a recumbent position.

In a group of 11 cases, 2 required anæsthesia, one being unreduced over a period of 48 hours and the other, a very muscular person, was reduced readily and with the first manipulation under anæsthesia. One outstanding case was a male weighing over 400 pounds, with a fracture dislocation. The dislocation was reduced at the first trial, without anæsthesia. Two men were required to lift the arm. The fracture also united with no apparatus other than a sling for the arm. Another case of fracture of the right humerus at the anatomical neck, where a moderate degree of angulation was in evidence, was corrected by the foregoing manipulation so perfectly that the line of fracture was with difficulty visualized in a post-manipulative x-ray film.

Theoretically this procedure could evoke discussion and criticism, but in practice it works like magic. Should any reader try this method, or if anyone has a series of cases in which this method has been used, I would be pleased to have his impressions.

I am indebted to the late Dr. Dalton Smith, of Mitchell, for the first demonstration in 1917, and I believe that he used this plan of reduction for a number of years, having had it passed on to him by one of his predecessors. The Kocher method may be all right for those who have taken memory courses, or the unshod foot and pull business for the especially graceful, but the method here described calls for a minimum of effort and pain.

I have an idea that this method of reduction must be known to bonesetters and older country doctors (as was hanging a patient by the arms from the top of a door), but why does it never get into a textbook or the teaching in schools? Either it is not known or is considered dangerous.

At times I have seen failure in the reduction of fracture-dislocations, even after pins and weights have been used. Operation has been done and the cancellous head of the humerus cruelly damaged by prying chisels, when pulling the arm straight up above the body in full extension would have so easily brought the fractured ends into proper position.

THE DIAGNOSIS OF APPENDICITIS.—W. J. Crocker and E. H. Valentine state that a more accurate diagnosis of appendicitis can be made by a modification of Schilling's method than by the use of any other white cell study. In the Schilling method, which is more complete than the usual Ehrlich technique and simpler than the Arneth count, the neutrophils are divided into four groups based on their maturity—namely, myelocytes, juveniles, stabs, and segmenters. Normally there are in the peripheral blood approximately 5,000 neutrophils per c.mm., distributed as follows: myelocytes nil, juveniles nil, stabs 4 per cent, segmenters 64 per cent. Schilling calls myelocytes, juveniles, and stabs "shift cells". Except for 4 to 10 per cent stabs, these cells are absent during health but may appear during infections; an increase in the number of "shift cells" with a decrease in the segmenters is called a shift to the left, and indicates that the severity of the infection is increasing. Where the opposite occurs and there is an increase in the number of segmenters, this is a shift to the right, and indicates that the infection is subsiding. Five hundred cases of appendicitis were studied clinically and by this method, and it was possible to distinguish between eight degrees of infection or pathological states of the appendix. The modified Schilling neutrophil count is presented, not as definitely diagnostic, but as a valuable aid to diagnosis that can be supplied by the clinical laboratory. The limitations of the simple "white cell count and differential" in this respect have long been recognized. If the "hæmogram" is carefully studied in the light of clinical data accurate diagnosis of the degree of appendicitis may be made in about 90 per cent of cases.—*J. Lab. & Clin. Med.*, June, 1936, p. 883. Abs. in *Brit. M. J.*

Editorial

CHOREA

THE arresting question has been asked rather recently in regard to chorea—"Is it a manifestation of rheumatic fever?"[1] There is now and there has been for a long time a widespread feeling that it is, or, to put the matter somewhat differently but perhaps more correctly, that, like rheumatic fever, chorea is dependent on infection with a streptococcus. Poynton and Schlesinger,[2] recognized authorities, have no doubt as to the answer. They say "Chorea is now looked upon as a rheumatic lesion" (*loc. cit.*, p. 66). They also speak of chorea as "cerebral rheumatism". They qualify their statements, however, by saying "It would be unwise to state that all cases of chorea were rheumatic, for on rare occasions tuberculous meningitis, encephalitis, and congenital syphilis simulate chorea". It would clarify the whole subject, it may be remarked here and now, if we were to realize that "chorea" is not a disease entity but only a clinical syndrome. Chorea, in that sense, then, may be a manifestation of one or other of several infections which are alike in this, that they attack the same areas of the brain. Nevertheless, admitting this, it would seem that rheumatism, acute, chronic, or latent, is the condition by far the most frequently associated with chorea. Certainly, if we could only settle on one specific micro-organism at work in both the matter would be settled beyond extreme probability. Further, Poynton and Payne (*loc. cit.*, p. 22) hold that chorea is the most frequent solitary manifestation of acute rheumatism, and that it is also the most obvious clinical index of rheumatism in childhood during school life.

Opposed on the matter are Gerstley and his associates.[1] Basing their opinion on a study of 150 patients, having regard to their social and economic situation, their clinical records, and the physical findings, as compared with a control group, they found nothing to suggest a close etiological relationship between rheumatic fever or any specific infection and chorea. A clear-cut history of rheumatic fever was obtained in only 6 cases; 14 others gave a doubtful history. In only one case of chorea with tonsillar trouble and without a history of rheumatic infection did endocarditis develop. These workers conclude—"Chorea may be caused by rheumatic fever, but this is only one of many immediate causes. Psychic trauma seems far more important." Where lies the truth?

On clinical grounds alone there are strong reasons for identifying chorea with rheumatic fever. First of all is the frequent association of the two conditions in the same individual. Poynton and Payne (*loc. cit.*, p. 22) refer to 1,108 recorded cases of first attacks of rheumatism in children under twelve years of age 613 of whom also manifested chorea. Combined statistics from Philadelphia and Baltimore show that 21.6 per cent of their chorea cases had a history of rheumatism.[3] Chorea may precede, accompany, or follow attacks of rheumatic fever. Both conditions also show a relationship to scarlet fever (probably a streptococcal infection). Both are common in children and young people. In the case of chorea females are affected more often than males, in the proportion of 71 to 29 per cent. In rheumatism, below the age of twenty, females also predominate. The following conditions are common to both chorea and rheumatic fever—fever, diseased tonsils, endocarditis, pericarditis, arthritis, subcutaneous nodules, erythema nodosum, meningitis, though the frequency of incidence is not identical in the two cases. The most common of these is endocarditis, and this statement is applicable to both chorea and rheumatism, as will readily be admitted. All this strongly supports the view that chorea and rheumatic fever are essentially the same thing.

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Without asserting that the matter is finally settled, all the available evidence goes to prove that rheumatic fever is due to an infection, either directly or by way of allergy, and that the lesions thereof are inflammatory. There are reasons for thinking that chorea should come into the same category. In both cases some form of streptococcus has been incriminated. Quigley[4] in 21 uncomplicated cases of chorea obtained 10 positive blood cultures in 9 of which streptococci were isolated. Streptococci were also found in the cerebrospinal fluid in 13 cases. Again, Rosenow[5] claims to have produced chorea in animals by the intravenous injection of a streptococcus obtained from the blood in a fatal case of chorea. He also produced experimental chorea with streptococci isolated from the tonsils in acute cases of chorea. This particular microorganism produced arthritis and carditis in rabbits. Control experiments with other micrococci gave negative results. Such observations are highly significant.

The lesion at work in chorea was thought by Henrici (1916), on the basis of experimental work in rabbits, to be a sub-acute meningo-encephalitis. Naturally, in the case of the human subject, opportunities to test this conclusion are rare, inasmuch as relatively few cases of chorea end fatally. Greenfield and Wolfsohn,[6] however, have made a detailed histological examination of the brain in a fatal case of chorea. The lesions were widely distributed and everywhere above the pons there were evidences of slight encephalitis. There was some infiltration of the pia-arachnoid, but this was not a striking feature. Their finding of thrombi in certain of the bloodvessels recalls Bastian's thrombosis theory,[7] first promulgated in 1869. Ziegler[8] has reported on a similar case. That chorea is due to a meningo-encephalitis would seem to be proved, and this view best explains its clinical characters. The association of a streptococcus, also, links it up closely with rheumatic fever. Could Aschoff bodies be demonstrated in the tissues in chorea valuable corroborative evidence would be obtained. That chorea can be produced by other infections would seem to be indicated by the fact that it has been found associated with tuberculosis, gonorrhœa, congenital syphilis, the puerperium, epidemic encephalitis, and some cases of sepsis.

The question asked at the beginning of this editorial must, in our judgment be answered in the affirmative. The statistics adduced to prove the opposite are not convincing. To settle a question like this a greater number of cases must have been examined. We know, too, that the incidence of rheumatic fever and chorea varies greatly in different countries. It is very high in the British Isles, for example, and very low in certain parts of the United States. Naturally, the conclusions based on a great number of cases, and particularly when many of these cases are of a severe character, are likely to be more correct. The finding of a streptococcus in cases of chorea and the clinical similarity of chorea and rheumatic fever are strong arguments in favour of identity. Saying this, however, but bearing in mind that chorea is merely a clinical syndrome and not a disease, we may admit that in rare cases chorea may occur without relation to rheumatism.

A.G.N.

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ON WRITING FOR MEDICAL JOURNALS

IT has been said, on sufficient authority, that "a policeman's lot is not a happy one". Neither is an editor's, though there are mitigations. We sometimes feel that an editor is conceived of as a sort of autocratic Jupiter whose thunderbolts have been replaced by scissors and paste-pot. Such, however, is not the case; an editor is one of the most genial of men! He may have his exasperating moments, but his sense of humour comes to his aid, and all is well. The duties of an editor are, of course, to edit, and this means that he must select from the manuscripts submitted to him for publication those that are suited to the needs of his journal; he must see that the articles are in proper form for publication (spelling and grammar attended to!); and he must provide a suitably varied menu. These reflections are prompted by the perusal of a supplement to *The Lancet* for January 2nd entitled, "On Writing for The Lancet". This supplement contains much meat, and we are heartily in accord with most of the recommendations and requirements of our brother editor. We wish that we could print his remarks in full, but, short of this, commend them to our readers and, particularly, to our writers. We shall, however, emphasize certain points that appeal to us.

Writing is an art, but so far as scientific articles are concerned that art should be restricted to telling the story accurately, simply, clearly and concisely. There is no place here for rhetoric, fancy, or inflated periods. While admitting that "Jove sometimes nods", or, as the Editor of *The Lancet* puts it, "admitting the insecurity of people who live in glass houses", we venture to offer some suggestions, which, if heeded, will make the editors' lot a happier one.

Papers should be as short as possible. Short papers are more likely to be read and more likely to be published. Yet, much depends upon the subject and the manner of presentation. As the Editor of *The Lancet* remarks, some papers of 500 words are long and others of 5,000 words are short. Most papers, however, can be shortened by at least 20 per cent by the avoidance of repetition, tautology, and pompous circumlocution. Printing costs money, and wasted space is a dead loss financially, not to speak of the increased tax on library space, which has now become a pressing problem. A good plan to adopt, after writing an article, is to put it away for a time and ask the opinion of your candid friends. When you take it up again you will be surprised to find how much you can improve it. Avoid medical jargon and "newspaperese". Write straightforwardly, in words that anyone can understand. Do not use a Latin or a Greek word when a plain English one will do. Resist any tendency to high-falutin language. Here, as elsewhere, fine feathers do not make fine birds.

There are some elementary rules that are frequently ignored. All manuscript intended for publication should be typewritten, *double-spaced*, and the original copy sent in. Otherwise, the work of the editor is doubled and the time of the printer wasted. Do not use abbreviations. L.O.A. and B.M.R. may be intelligible to most readers, but some others may not. Photographs for reproduction should be unmounted, marked as necessary on the back, and be accompanied by the proper legends on separate sheets. Avoid as far as possible writing on the face of the photographs. If this must be done, see that the lettering is sufficiently large that when the picture is reduced it will be legible. Be particularly careful in regard to bibliographies. The items should be arranged alphabetically and numbered consecutively. See that reference is made by proper number in the text. The author's name with initials, should be given, followed by the title of his paper, the name of the journal in full, the year, volume number (underscored), and the first page number. Above all, check the references to see that they are correct. An incorrect reference is worse than none, for it is misleading. This caution is very necessary, as we frequently find gross errors here. A concise summary is very desirable; it is often the only part of the paper that is read. A consummation highly to be desired is that a paper should be in such form that it could be sent to the printer without change. Such a marvel, however, we never expect to see.

Like the Editor of *The Lancet*, we have certain pet aversions. We admit to all his, and more. The word "case" is often used as synonymous with "patient", man, woman, or child. A "case" is impersonal; it is an account of a "patient's" ailment, not a person. You cannot operate on a case. Do not say, "the patient was 'operated' "; he was "operated *on*". Do not say "pathology" when you mean "lesion". "Pathology" means "a treatise on disease" or an account of disease processes. Do not, therefore, write "there was no pathology in the pelvis". The term "acute abdomen" is absolutely wrong, but is, admittedly, convenient. We fear it has come to stay. We have even met with its legitimate offspring in "the acute pelvic woman"! "Individual" is frequently used when "person" or "patient" is meant. A person is an individual only when that person is considered in his relation to a larger group or a community. The word "meticulous" is a favourite with the newspapers and those who copy them. It is derived from the latin *meteo, I fear*, and is not appropriate when used, as it commonly is, for "painstaking care". "Appendicectomy," though an objectionable hybrid term is, at least, better than "appendectomy". "Therapy" is a great favourite just now. It means "treatment", so why not use the plain English word? We are even treated to "treatment by radium therapy"—a splendid tautology! We are indeed beginning to think that therapy is a more "blessed" word than Mesopotamia. Then, there is our old friend "consensus of opinion". Consensus is sufficient; it means in itself the opinion of a majority of persons. Only, we pray that we may not be afflicted with "concensus of opinion". "Consensus" has nothing to do with "census". Anyone who uses this phrase is convicted of illiteracy, even if he is an M.D. "Pruritis" is frequently used instead of "pruritus". Do not use "pubis" as subject instead of "pubes". "Pubis" is the genitive case. You need the nominative.

A bad fault that we often meet with is to intermingle singular and plural forms, thus—*A* person (singular) does not realize what may be coming to *them* (plural). This is ungrammatical and bad form. Another fault, not so objectionable, perhaps, is changing the construction in subordinate clauses from that adopted in the principal clause—changing from a finite verb to a participle, for instance. Grammar, like spelling, should be impeccable.

Another pet aversion is what has been called the "telegraphic style" of writing. This style is staccato; the definite and indefinite articles are frequently omitted, sometimes, the verbs; little or no respect is paid to punctuation. The whole is reminiscent of a badly taken case report in a hospital record. The effect is sloppy.

The use of paragraphing and of A.B.C., a.b.c., and (1), (2), (3), "reminiscent of examination answers, can certainly be overdone". The Editor of *The Lancet* puts it drolly, that "Shakespeare, if a surgeon, would probably have written: '(1) To be, or (2) not to be; that is the question. Whether 'tis nobler (a) in the mind to suffer . . .' "

A good plan for writers to follow is for them to study the journal to which they propose to offer their contributions, and to follow the form adopted therein. This form will cover centre headings, side headings, italicizing, spelling, and probably other things. In the matter of spelling the *Canadian Medical Association Journal* follows the Oxford Dictionary, with rare exceptions.

When all is said and done, we gladly admit that the quality of the material offered us for publication is steadily improving. We sometimes receive papers that are a joy to read; they are clear, logical, grammatically expressed, and well displayed. A.G.N.

A NEW AIR-DRIVEN ULTRACENTRIFUGE.—J. Biscoe, E. G. Pickels, and R. W. G. Wyckoff describe a new type of centrifuge driven by an air turbine which they have built up in their own workshop at a cost very much less than that of the well-known Svedberg oil-turbine machine. Briefly, it consists of a duralumin rotor of a size sufficient to allow of a distance of 6.5 cm. between the centre of the cell to be centrifuged and the rotation axis. The rotor is driven by a turbine operated by compressed air. In practice air was taken from the ordinary house line at a pressure of about 100 lb. per square inch and reduced by an automatic regulator to a constant pressure of 40 to 50 lb. per square inch. The material to be centrifuged is contained in quartz cups, so that photographs can be taken in ultraviolet light during the process of centrifugation, and the extent to which the particles are being thrown down registered in much the same way as in an ordinary red cell sedimentation test. The cups are contained in a special chamber from which the air is evacuated so as to diminish friction to a minimum. Speeds of about 50,000 revolutions per minute are obtainable with this centrifuge.—*J. Exper. M.*, July, 1936, p. 39. Abs. in *Brit. M. J.*

Editorial Comments

Progress in the Study of Influenza

It is now nearly four years since Smith, Andrewes and Laidlaw announced that they had obtained a virus from influenza patients.[1] While their discovery has been confirmed, yet this has been so under considerable difficulties. It has been found that the virus can be obtained only from cases occurring at times of epidemic and not from sporadic cases. The research worker is therefore hampered by this fact, though, it is true, matters have been better since it was discovered that influenza could be induced in ferrets and be transmitted through them to mice. This has made it possible to maintain the virus for some time and study the reactions that it sets up.

The recent extensive epidemic of influenza in England has afforded Hoyle and Fairbrother[2] an opportunity to examine these questions further and they confirm the view of Smith, Andrewes and Laidlaw that influenza is due to a virus. In view of the well-known fact that there are two related but distinct strains of the influenza virus—human and porcine, it was of some importance to determine which was at work in the recent epidemic. The identification was carried out very satisfactorily by quantitative neutralization tests in mice. Hoyle and Fairbrother found in the Manchester epidemic, which was the one they studied, that the human type of virus was the form at work, and there was nothing to indicate that any other pathogenic organism (in particular, *H. influenzæ*) was associated with it. Where it was possible to examine the blood serum before and after an attack of influenza it was found that an increased titre for antibody was present in the case of convalescent patients as demonstrated by the complement fixation test. Their results also suggest that persons with a low antibody titre are more susceptible to infection than those with a high titre.

The complement fixation test provides a possible method for differentiating immune from susceptible persons that will prove of value when it becomes possible to introduce prophylactic vaccination, which would seem to be just in the offing. For Francis and Magill[3] have been able to produce a decided rise in the antibody titre by the subcutaneous injection of the living cultured virus without causing any signs of infection. These workers suggest that this increase in the antibodies is accompanied by an increase in the ability to resist an original influenzal infection. A.G.N.

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The Late Sir George Washington Badgerow, C.M.G., C.V.O., M.D.(Tor.), F.R.C.S.(Edin.)

Sir George Badgerow, a well known specialist in diseases of the ear, nose and throat, and a prominent member of the Canadian colony in London, died suddenly in a taxi on May 9th, as he was driving to Waterloo Station.

George Badgerow was born near to Toronto in 1872, the son of W. A. Harrington Badgerow, and received his early education at Upper Canada College. He studied medicine in the University of Toronto, graduating M.B. in 1894. He practised in Toronto for five years, holding the position of surgeon in the Toronto General Hospital. Going to England in 1900, he continued his studies at University College Hospital and Middlesex Hospital and received the F.R.C.S. of Edinburgh in 1910. Devoting himself to his specialty he became attached to the Throat, Nose and Ear Hospital, Golden Square, London, with which institution he was connected in some capacity or other for the rest of his life, latterly as consulting surgeon. He served for a number of years as dean of the attached school of medicine. Sir George held many professional appointments at various public institutions and was especially active during the Great War. For his eminent services he was made C.M.G. in 1918, was knighted in 1928, and given the C.V.O. in 1930. He was an officer of the Order of the Hospital of St. John of Jerusalem in London.

Sir George was a busy consultant and found little time for literary or social activities. He was not a frequent writer on medical topics, nor was he a consistent attendant at medical meetings, but he was highly regarded nevertheless for his scientific attainments and for the thoroughness with which he carried out any duties upon which he entered. He was greatly esteemed by all who knew him intimately and particularly by his fellow Canadians. He had been for many years a member of the Canada Club, and recently was prevailed to take on the duties of its honorary secretaryship. A.G.N.

Retrospect

THE NON-SURGICAL CURE OF CANCER

BY DANIEL NICHOLSON, M.D., M.R.C.P.(LOND.)

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Because there are many forms of cancer in which surgical excision does not yield a cure there has always been keen striving for other effective forms of treatment. Soon after any new chemical, bacterial or biological product or physical force was discovered its effect was tried on cancer. In this paper I shall discuss constitutional therapy in cancer other than radium and roentgen ray, which are accepted adjuvants to surgery.

In assessing the value of any therapeutic agent everything depends on the standards used in judging the results. The earliest attempt to present the end-results in the treatment of cancer in a comprehensive manner came from Billroth's clinic in Vienna. In 1878 his first assistant, Von Winiwarter, published a study of 548 patients with carcinoma on whom surgical operations had been done from 1867 to 1876. Out of 170 cases of cancer of the breast 4.7 per cent were alive and well three years or more after surgical operations.[1] Since that date the surgical cure of cancer has been greatly enhanced by the education of the public regarding its habits of growth and by the increased knowledge of surgeons in pathology and operative technique. Today's surgeons, realizing the slow and irregular growth of cancer, judge their results on the percentage of early and late cases that are free from all signs of recurrence 5 or 10 years after excision or radiation. This rigorous but necessary standard for judging results has not been generally adopted by those applying non-surgical methods. The result of most hypodermic treatments, whether they are of mineral, vegetable or animal origin, can be grouped together, although they may vary greatly in some instances. Lasting one to three months, sometimes longer, the following occur. (1) After an initial short period of increased pain or a sensation of drawing in the tumour there is dramatic relief so that the patient may sleep well with little or no morphine. (2) The appetite improves, the patient gains weight, and loses the cachectic appearance. (3) In less than half the cases there is diminution in the size of the tumour, with softening at its margin, sometimes throughout. Occasionally this is very striking, but after a few weeks of improvement the patient's condition resumes the downward trend. Many show no effect whatever.

Unless a physician is acquainted with these phenomena he cannot escape the conviction that cure is beginning. The blood supply of all tumours is very uneven, and rapidly growing tumours have very thin walled imperfect blood vessels which rupture or become thrombosed more readily than normal body capillaries when subjected to toxic influences. The infarcted area within the tumour undergoes autolysis and the liquid part is absorbed. The injected substance and the necrotic tumour tissue stimulate the production of macrophages which phagocytize dead and dying cells. So the tumour softens and temporarily diminishes in size. But many areas survive and continue their malignant growth. Consequently the patient's life is prolonged little if any. Very rarely the whole tumour may be destroyed, but this occurs so infrequently that no therapeutic reliance can be placed upon it. Many times there is no apparent effect on the tumour or its rate of growth. Obviously, if the body does not react to the substance injected no benefit accrues.

In considering any temporary symptomatic benefit that may occur in the patient and the rare occasion of a cure, one should not lose sight of the fact that these medical remedies for cancer in many instances postpone the opportunity for the more certain cure by surgery and radiation until the cancer has reached a late incurable stage. With the high degree of development of experimental methods today the therapeutic results in cancer-bearing animals should be excellent before the remedy is tried on human beings.

For the sake of convenience we can divide non-surgical attempts to cure cancer into three periods, although they overlap considerably. Up to 1880 was the period during which most of the inorganic chemicals were first tried out both locally and internally. From 1880 to 1900 most of the bacteria and their products were tried out. The third period from 1900 to the present day is an experimental stage in which animals are used. Only a few of the products in any of these groups can be listed and but one or two representative ones given in outline. Many of the present familiar compounds of acetic acid,[2] arsenic,[3] hydriodide of potash,[4] bromine,[5] copper,[6] lead,[7] magnesium sulphate,[8] potassium chlorate,[9] turpentine[10] and a host of other chemical substances were tried out during the first period. Temporary shrinking of the tumour and improvement in the patient was noted in a number of instances. About 100 years ago the mixing and application of arsenic pastes was a fine art, and although it cured superficial cancers it was generally agreed later that surgical excision, using aseptic methods was preferable.

Lead held by far the most prominent place among the metals used in the therapy of cancer. It was tried out extensively in the eighteenth century.[7] Shrinking of the tumour was noted in some instances and absolute cures claimed in a few. It was finally abandoned, only to be taken up again by Professor Blair-Bell, of Liverpool, following the world war. The number of papers published on this subject since that time has been

enormous. Their number reached an all time peak in 1929, followed by a remarkable slump in 1930, quite similar to the curve showing the quotations on the New York stock exchange for that period. Again, to maintain this parallel, the number of papers on lead therapy are now increasing. At the Mayo Clinic they have recently used it on some incurable cancer patients, and observed regression and freedom from signs of recurrence for at least two years in about 20 per cent of cases, when combined with surgery and radiation.[11] The general toxic effects of lead are very severe. To lessen these, the lead has been incorporated into sugar compounds.[12]

Before the isolation of bacteria, cancer patients were inoculated with various infectious diseases in the hope that the growth of the cancer might be checked. Even inoculation with syphilis has been tried.[13] In the older medical writings there are descriptions of the regressions which occurred in the malignant tumours of some patients who developed erysipelas.[14] Prompted by his observation of this phenomenon Dr. W. B. Coley, of New York, injected hypodermically living broth culture of *S. erysipelatis* and obtained some remarkable cures. Because of the severe and dangerous reaction he later used a vaccine of killed organisms of *S. erysipelatis* and *B. prodigiosus*. As early as 1896 he published extensive reports on 160 cases of carcinoma and sarcoma treated by his toxin.[14] Out of 17 of his own cases of primary and recurrent carcinoma 3 were permanently cured, and 10 showed a temporary regression of the tumour. Out of 17 cases of sarcoma the tumour disappeared in 7 and the patients were free of recurrence for periods over 1 to 7 years. He concluded that action of the toxin on sarcoma was three times as marked as on carcinoma, but he later abandoned the treatment of carcinoma by this method, though he continued to use it in sarcoma, mainly of bone. The most favourable results followed injections of virulent cultures which produced a severe reaction. His excellent report of 40 years ago will repay one reading it today. The Coley toxin is approved by the Council of the American Medical Association but is not in common use.

Following the development of culture methods for bacteria tumours were assiduously subjected to a great variety of cultural methods in the hope that an etiological organism might be discovered. Many different organisms were found and disputes followed regarding their significance. Perhaps the one which had the greatest following was a micrococcus reported by Doyen[15] in France. He found it in benign and malignant tumours. Its cultural characteristics were like the *Staph. albus*, except for a stringy consistency of its colony. He gave it the attractive name of "*Micrococcus neoformans*". Scores of physicians were favourably impressed with this vaccine. In America favourable results were reported in the eastern United States from the use of this vaccine as recently as 1911. In far advanced cases the most consistent effect was marked relief of pain, an improved general state of health, gain in weight, appetite and strength, and loss of characteristic cachexia. Narcotics could be stopped. When the vaccine was discontinued the patients again became restless, the pain returned or increased, and insomnia and anorexia developed. If the dosage intervals were lengthened the patients stated they could feel the effects wear off. There was no diminution in size of the internal masses, but the superficial ulcers became clean. One author remarks that "when such results could be obtained in advanced inoperable cases what might we not expect in early cancer treated with this vaccine together with surgery".[16] Later investigation showed that this organism was an ordinary staphylococcus. The results observed following its hypodermic injection may be obtained by the injection of many other foreign protein materials.

As a vegetable product used in treating cancer, carcinolysin, an extract of the Chinese plant "haising" dissolved in oil, and administered hypodermically, has had a very extensive use. It is said to contain a ferment which is harmless to healthy tissues or bacteria but has a destructive effect on carcinoma cells. In primary carcinomatous tumours of experimental rats and rabbits softening is first noticed, then necrosis, and finally absorption. The combined observation of Japanese doctors on 3,417 cancer cases showed that 26 to 35 per cent of the cases showing active growth were cured.[17] When it does not cure it relieves pain and offensive discharge. In commenting on carcinolysin Dr. Blumenthal, director of the Institute for Cancer Research of Berlin, stated the result of treatment with this remedy is practically the same as the medical carcinoma treatments with a great many remedies. It brings on a forceful softening of the tumour and may hasten death. Occasionally the tumour disappears, but more often it cannot be stopped. In most patients suffering from carcinoma after receiving carcinolysin there is not only a general reaction but also a local painful sensation in the tumour, inflammation, softening, and then breaking down of the tissues. If carcinolysin in occasional cases appears to have favourable reactions it is not specific and the question is whether the preparation has enough advantages in comparison with other medical methods of treating carcinoma that one should make use of it.[18]

Early in this century, when pioneer developments in x-radiation and radium were taking place, extremely valuable experimental methods on animals were also developed for the investigation of cancer. The mouse and the rat were chiefly used, the rat for tumour transplants and the mouse to produce a high incidence of cancer of the breast by inbreeding, to develop tar cancer, and to work out problems in

heredity.[19] Cancer of the stomach was first produced in a rat experimentally by a Spiroptera worm in 1913. Skin cancer was produced on a rabbit's ear by tar in 1915, and sarcoma of the liver by the cystic stage of the cat tapeworm in 1920. The life span of the mouse is less than 1/20 that of a man. Therefore much information regarding its cancers may be found out in a short time. It is now no longer necessary to use man as an experimental subject to test the efficiency of new treatments for cancer.

However, in assessing results in animal experiments one encounters difficulties. Most experimenters use too few animals in their series and inadequate controls. Infections are more potent causes of death in cancer mice than the cancers themselves, a point not often realized. The unnecessary repetition of previous well done experiments is enormous. To conduct sound experimental work in cancer research requires an apprenticeship at a reputable institution for two or three years like any other specialty in medicine.

The discovery of vitamins led to much experimentation on the effects of various diets in cancer. This research was intensified by the effect of liver in pernicious anæmia. In 1922 the effect of a diet free from fat-soluble vitamin A was tried on cancer patients, on the basis that the young embryonic cancer cells would suffer more than adult cells of the animal's organ. The results were negative[20] and were later confirmed.[21] Massive doses of vitamin A were found to have no effect on rats bearing the Walker carcinoma.[22] The effect of cod liver oil was tried in 1925 with negative results in Flexner-Jobling rat carcinoma and the Bashford and Twort mouse carcinoma,[23] but in 1936 the feeding of cod liver oil resulted in only 76 per cent of the amount of growth present in control animals.[24] An increased carcinoma development was observed in tar-cancer mice when their diet was supplemented by liver.[25] Later, more detailed experiments[26] show that liver, pancreas and intestinal mucosa promote the growth of tar cancers in mice, while brain, thymus, bone marrow, dried gastric mucosa and dried lymph nodes have an inhibiting action. The tumour stimulating substances appear to be water-soluble and the tumour-inhibiting substances are ether soluble but they do not produce regression in tumours already developed.

In 1933 Marchesi[27] found that administration of wheat-germ oil (vitamin B and E) produced no influence on growth of Jensen rat sarcoma. Subcutaneous injections of wheat-germ oil both into animals having a carcinoma and sarcoma did not influence the course of the malignancy in either disease. Dr. J. R. Davidson has found that mice fed on high vitamin E diets (wheat germ) develop tar cancers less readily than do mice fed on a low vitamin E diet.[28] As a general observation Dr. K. Sugiura[29] has stated that tumour growth is greatly retarded when the animal is maintained on the verge of starvation, but when normal feeding was again resumed the tumours again started to increase rapidly.

Many bacterial extracts have been tried out on experimental cancer animals. Toxic filtrates of typhoid cultures,[30] meningococci[31] and *B. coli*[32] have been injected into many cancer-bearing animals, and in many instances a regression of the tumours occurred, but the large doses necessary for this destructive effect in a high percentage of cases sometimes proved fatal to the life of the animal. The effect is somewhat the same as that obtained by Coley's vaccine.

At the Memorial Hospital in New York, Torrey and Kahn from 1924 to 1927 experimented on cancer with *B. histolyticus*.[33] Both filtrates and thin cultures of this bacillus grown on beef broth were injected into adequate series of rats bearing Flexner-Jobling rat carcinoma. Destruction of the tumour occurred only when the injections were made directly into the tumour. The culture was more proteolytic than the filtrate. Any substance resulting from the action of this bacillus on the tumour cells would be produced in enormous quantities, and if it had a destructive effect on the tumour this should be very marked. This did not occur, as some of the tumours recurred locally and in a few instances metastases continued to develop. Immunity to the organism developed after 7 to 10 days, which rendered subsequent injections ineffectual. The clinical staff of the Memorial Hospital did not see fit to use this method on human cancer patients.

Culturing the same organism on cancer tissue in a test tube and filtering to produce a sterile solution, which he called "ensol", Connell in 1935 treated cancer patients after a few apparently encouraging animal experiments.[34] The treatment of cancer mice by ensol when repeated by Dr. Gye, Director of the Imperial Cancer Institute in London showed no curative effect.[35] Due to widespread publicity 672 patients have sought this treatment and 488 have been treated. Some regression of the tumour was reported in 34 per cent and amelioration of symptoms described in more. The foreign protein or toxic reaction, which is severe after the injection of most bacterial products, is mild or absent after the use of ensol. Not enough time has elapsed to prove permanent clinical results but the general impression is that this remedy lacks sufficient value to justify its use. The experiments of Torrey and Kahn and those of Connell have many features in common, except that in the former all the process takes place *in vivo* while part of the latter is *in vitro* and the doses of the resulting substances are very much smaller.

The number of protein products tried in the treatment of cancer has been enormous: the ultra peptones of cancer,[37] cancerous autolysates,[38] decomposition products of tissue and bacteria by fermentative processes,[39] trypsin solution,[40] and hormones.[41] Hypodermic injections of adrenalin, splenic, ovarian, corpus luteum, pituitrin and gonad-stimulating principle were given to experimental animals bearing R-10 sarcoma and Hyde carcinoma.[41] Although some extracts induced early liquefaction, no appreciable effect on tumour growth or incidence of mortality was observed.

Many attempts have been made to produce a serum against cancer. Clinical benefit has been claimed following the administration of goat serum and oleates,[42] and even following simple autoserotherapy, that is, the re-injection intramuscularly of 20 c.c. of the patient's own blood.[43] The reaction from these has undoubtedly been that of a non-specific protein. Lumsden has inoculated sheep with mouse carcinoma to produce a serum against cancer in mice. Seventy-four per cent of spontaneous cancers of mice were cured by the injection of euglobulin fractions of the anti-serum around the cancer.[44] Lumsden's work has been criticized[45] on the basis that he was merely producing antibodies against mouse tissue in general, but recently he has demonstrated the formation of antimalignant cell bodies in the serums of rats inoculated with rat sarcoma, that is in a homologous serum.[46] This would represent the experimental production of the phenomena observed by Dr. Hodenpyl[47] whose patient developed, following breast carcinoma, liver metastases, which latter regressed but produced large quantities of ascitic fluid. When this fluid was injected into other cancer patients it produced remarkable regression in the tumours.

On the basis that the thymus and spleen rarely harbour cancer and that the large thymus of infants is antagonistic to epithelioma, Fichera made extracts of these organs and injected hypodermically patients having recurring breast or rectal cancers or lymphosarcoma.[48] He shows most convincing biopsy microphotographs illustrating the progressive stages of the malignant-cell destruction. Although in 300 inoperable cancer patients he describes total tumour disappearance in 9 per cent and arrest in 8 per cent more, over a two to three year period, other experimentalists state that they cannot obtain any benefit from the use of his material. In contrast to Fichera, Meyer and Simmons report the treatment with thymus extract of 50 mice bearing experimental implants of carcinoma compared with 23 untreated controls.[49] No difference in the rate of growth or post-mortem appearance of the tumours was observed. Recently Blumenthal has observed striking early regressions in advanced inoperable human cancers following injections of extracts of *fresh* animal organs, but the cases have not been followed long enough to determine the ultimate outcome.[50]

After many years of experimental research on cancer Dr. J. B. Murphy, of the Rockefeller Institute, New York, took as a working hypothesis that cancer might be the result of the lack of some growth-controlling factor in the serum or tissues.[51] He also assumed that this growth-controlling factor, in order to produce the proper cell differentiation to form normal organs in the growing embryo, would be present in its greatest concentration in tissues having the greatest growth energy, such as placenta and embryo skin. Extracts from the placenta and skin embryo were injected intraperitoneally at weekly intervals into mice suffering from spontaneous cancer of the nipple. The results showed slightly more than one-quarter continuing to grow, slight retrogression in less than one-quarter, marked retrogression in one-quarter, complete, in about one-fifth. Mammary cancer in mice is a very malignant tumour. It begins as a papillomatous change in the nipple and goes on to produce an epidermoid carcinoma. The data regarding breast cancer in mice, its spontaneous regression, the recurrence after surgical removal or radiation, are remarkably uniform with different investigators; in fact much more so than our figures published on human breast cancer. Local recurrence following operation is ordinarily about 50 per cent, but if a small drop of the placental extract was sealed in the wound with collodion the recurrence was reduced to 6 per cent. The effect of the constituents extracted from the placenta are now being tested. The results are not considered sufficiently complete to warrant a clinical trial.

SUMMARY

1. The temporary improvement of the patient's condition and the shrinking in tumours following parenteral injection of many substances have raised false hopes regarding the recovery from cancer, and in many instances have caused the postponement of surgical excision and radiation.

2. The attempts to cure cancer by inorganic chemical substances were numerous previous to 1880. The main one persisting has been lead. The bacteriological era that followed produced one outstanding substance in cancer therapy, namely, Coley's toxin. From 1900 on the development of experimental methods in animals has removed the necessity of submitting human cancer patients to unsuccessful attempts to produce a cure except by excision or radiation.

3. A review of the medical remedies brought out during the last half century tends to make one critical of the value of any new one.

4. Although the structure of cancer is so plainly evident the reasons for its growth are so inaccessible that much investigation has yielded comparatively little specific knowledge regarding the effective control of its growth, except by excision or radiation.

The numbers in the text refer to a bibliography which will be listed in the reprints.

In Lighter Vein

ODE TO THE TONSILS

BY WILLIAM BOYMAN HOWELL

The otolaryngologist
Is wont with fervour to insist
That most of all the flesh's woes
Arise within the throat or nose.
He sings a song with this refrain:
"If you have any ache or pain,
Without the faintest trace of doubt
You won't be well till I take out
Your tonsils, your tonsils."

To all the world it is well known
That certain brats are very prone
To gaping mouths and vacant looks
And being stupid at their books.
By sniffing too, the angel child
Will often drive his parents wild.
Their love for him with hate's alloyed
Until he's lost his adenoid
And tonsils, and tonsils.

'Tis true that often catching cold
And mastoid ills must be enrolled
With other ailments more remote
Among the sins for which the throat
With no injustice can be blamed.
But many charges have been framed
Without a word of truth therein;
Slandering thus those organs twin,
The tonsils, the tonsils.

Some specialists, indeed, propound
The theory that you organs round
Cause maladies of every sort
From bandy legs to common wart.
Some of them have even seen
In you the cause of wand'ring spleen;
Of boils and bedsores, gout and sprue,
And lots of other horrors too.
O tonsils! O tonsils!

For three score years and something more
I've had no reason to deplore
The fact that I have never been
Bereft by glitt'ring guillotine
Held in a ravening surgeon's paw
Of those two guardians of my maw.
So since they've never been my bane
I think I might as well retain
My tonsils, my tonsils.

Association Notes

The Calgary District Association, Alberta Division, Canadian Medical Association

A meeting of this Association was held on May 27, 1937, at the Holy Cross Hospital. Dr. A. I. Danks, presided. An address on "Medical ethics" was given by Dr. J. K. Mulloy, of Cardston, one on "Acute intestinal obstruction", by Dr. Eardley Allin, of Edmonton. A motion picture, "Radium treatment of carcinoma of the cervix uteri" was shown.

Dr. J. N. Gunn showed motion pictures of the ski-championship events taken at Banff last February, also of well known golf players, and of fishing trips taken in the Rocky Mountains, which delighted his audience.

Hospital Service Department Notes

Group Hospitalization Reaches Million Mark

Membership in group hospitalization has increased three-fold during the past year according to Mr. C. Rufus Rorem, the Director of the Committee on Hospital Service of the American Hospital Association. A check of some seventy-five different organizations in the United States reveals a membership of approximately one million people. While Canada has a fair number of plans, few of these are located in large cities; hence the growth here has not been by any means so phenomenal as across the line. The growth in the United States has been largely among the non-profit plans offering free choice of hospital and of doctor—the type of plan recommended by the American Hospital Association, the American College of Surgeons, and by the Committee on Group Hospitalization of the Canadian Medical Association. Plans developed by private promoters or in connection with individual hospitals have not increased their membership on the average during the past year. A number of such plans have ceased activity, although no plan of the recommended type has been discontinued.

The most spectacular growth has accompanied the Associated Hospital Service, Inc., of New York. In its first two years of life, just completed, it enrolled more than 350,000 subscribers. The plan in Minneapolis and St. Paul has enrolled 85,000 in the past four years. Rochester, N.Y., now has over 65,000 members; Cleveland, Ohio, over 50,000; New Orleans, 40,000; Washington, D.C., 35,000; Durham, N.C., 26,000; Chapel Hill, N.C., 23,000; Newark,

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

N.J., 20,000; Sacramento, Cal., 16,000. All of these plans, particularly the New York plan, are growing by leaps and bounds, and would seem to be solving one phase of the problem of the cost of sickness.

These plans are by no means a complete solution; at best, they solve for the individual but one of the many costs of sickness, the hospital bill. However, that is one of the most formidable handicaps of sickness and the testimony of experience would now indicate a definitely satisfied and continuing membership, a medical profession pleased with earlier and easier hospitalization and better collections, because there is no hospital bill to interfere with professional payments, and a more satisfactory hospital budget. A large number of enquiries have been made in both countries by interested hospitals, medical men or prospective promoters, but plans have not been encouraged unless such emphasize public welfare, have non-profit sponsorship and control, offer free choice of hospital, embody community and medical representation, and are actuarially sound.

Reporting of Infections in Hospitals

With the greater study and analysis of clinical records in hospitals at the present time much better control of infections is possible now than hitherto, and efforts to track down the causes of infection and prevent spread to others are much more effective than in the past. Hospital staff meeting or service programs frequently contain a review of post-operative, obstetrical and other infections. Of particular importance is the necessity for having such regulations set up that immediately upon the recognition of an infection of possible danger to other patients the office and superintendent shall be notified, the attending doctor consulted, isolation technique adopted *pro tem.*, the chief of the service notified, and, if necessary, brought into consultation. In some hospitals a nurse attached to the operating room staff checks up on the ward for post-operative infections, thus facilitating prompt search for the flaw, if any, in surgical routine.

A very satisfactory arrangement for the reporting of infections is used in the Saskatoon City Hospital. A report form is used which is divided into four brief divisions. The first is for the *nurse's* report of her observations of any unusual sign or symptom developing. Not being medically trained, she does not state that this is an infection. This report is then immediately brought to the attention of the *intern* who fills in the second section, which asks "Is infection present or absent?", and furnishes a description of the changes observed. The third section is for the report of investigation by the *attending doctor*. The report is then placed upon the chart, and the Records Committee of the service concerned is required to comment on the report and bring it to the next staff conference of the service. The report of this conference is then noted on Section 4 of this report. Each of these four reports is dated and signed. With certain modifications in Section 4, and perhaps omission of Section 2, should there be no interns, the form could be utilized to advantage in hospitals of any size, and a prompt and thorough check thus made on all hospital infections.

Provincial Association Notes

The Manitoba Medical Association

The annual meeting of the Manitoba Medical Association was held in the Fort Garry Hotel, Winnipeg, on May 20, 21 and 22.

On May 19th the retiring President, Dr. George Clingan, of Virden, gave a dinner to the retiring executive, when the reports of various committees were considered and much business was done. On May 20th Dr. H. D. Kitchen spoke on "The importance of moderate degrees of hypothyroidism". Prof. F. T. Cadham spoke of the favourable effect of blood letting in donors of small amounts of blood. He based his remarks on observations made on children from whom blood had been taken to provide serum for patients suffering with infantile paralysis, and considered that the old practice of blood letting had its value. Dean A. T. Mathers discussed "The significance of common reflexes", and Professor Wm. Boyd spoke on "The cause of cancer". The speaker at the luncheon, when Hon. I. B. Griffiths, Minister of Health and Public Welfare, was present, was Mrs. E. L. Johnson, President of the United Farm Women of Manitoba. She spoke of the medical needs of rural Manitoba, and pointed out where she thought improvements might be made in providing medical care. She favoured the plan of municipal doctors and stressed the importance of the prevention of disease. In moving a vote of thanks to her Dr. J. D. Adamson suggested that the President name a committee to study her address and to report to the incoming executive, and such a committee was named.

In the afternoon Dr. T. I. Brownlee, of Russell, Man., spoke on the surgical training of the country practitioner. He urged that more training should be given to medical students which would enable them to carry out the simpler operations met with in rural practice. The health of the children in the Morden district was discussed by Dr. A. T. Menzies. He felt that the aid of agricultural experts and

veterinaries should be invoked to work in combination with public health officials and the medical men of the district to secure as favourable an environment as possible for growing children. Dr. W. A. Bigelow, of Brandon, discussed "Congenital bands of the cæcum and ascending colon", and Dr. C. R. Donovan spoke on "Prevention and treatment of poliomyelitis", while Dr. A. A. Murray discussed the prevention and management of deformities in that disease. Following the dinner that evening Dr. Clingan gave the presidential address.

The election of officers resulted as follows: *President,* Dr. C. W. Burns, Winnipeg; *First Vice-president,* Dr. E. L. Ross, Ninette; *Secretary,* Dr. D. J. Fraser, Souris; *Treasurer,* Dr. Digby Wheeler, Winnipeg. The resignation of Dr. F. W. Jackson, who for eight years had been Secretary of the Association, was received with regret.

Members of the executive at large elected at this time were: Drs. W. S. Peters, Brandon, and Earl Stewart, Winnipeg. Dr. W. G. Campbell, Registrar of the College of Physicians and Surgeons, gave an account of the activities of the College. Twenty thousand dollars had been set aside for the Gordon Bell Memorial Fellowship for research and large grants had been made each year to the Medical Library. The expenses of speakers at district meetings and at meetings of the United Farmers of Manitoba had been met by the College. A taxing committee to supervise accounts had been set up.

On the morning of May 21st surgical clinics were held in the Winnipeg General Hospital under the chairmanship of Professor J. A. Gunn. Surgical cases were presented by the following members of the staff of the General Hospital: Drs. G. S. Fahrni, A. C. Abbott, P. H. T. Thorlakson, C. W. Burns, M. R. MacCharles and W. A. Gardner.

St. Boniface Hospital was the host at a luncheon, and this was followed by a symposium on "Respiratory sepsis" under the chairmanship of Dr. J. D. Adamson. The contributors were Dr. E. L. Ross, Superintendent of the Manitoba Sanatorium, Ninette, Drs. Lennox G. Bell, D. L. Scott and D. S. McEwen.

The annual dinner and dance was held at the Fort Garry Hotel. On Saturday a golf tournament was held at Niakwa Club. Dr. Alex. Meindl was the winner of the Winnipeg Medical Golf Cup; Dr. Claude McRae won second prize; and Dr. R. W. Richardson, third. For the non-golfers clinical demonstrations were given on pneumothorax at the Central Tuberculosis Clinic by Dr. D. L. Scott and at St. Boniface Sanatorium by Dr. J. D. Adamson, while Professor D. Nicolson illustrated practical laboratory methods at the Medical College.

The Ladies Committee of the Manitoba Medical Association served tea at the home of Mrs. C. W. Burns on May 20th and 21st. Mrs. George Clingan entertained the wives of the retiring executive at luncheon at the St. Charles Country Club. Tours of the University and the Art Gallery were arranged for those interested. There was an interesting array of commercial exhibits at the hotel, the following firms being represented: Braithwaite's Ltd., Fisher Burpe Ltd., H. G. Fisher & Co., Robert S. Ramsay and the Winnipeg Drug Co.

ROSS MITCHELL

Medical Societies

The Calgary Medical Society

At the annual meeting of the Calgary Medical Society held April 13, 1937, the following officers were elected for the 1937-1938 session: *President,* Dr. A. I. Danks; *Vice-president,* Dr. E. A. Roach; *Secretary,* Dr. M. G. Cody; *Treasurer,* Dr. J. A. Reid; *Librarian,* Dr. G. E. Learmonth; *Executive Committee:* Drs. L. G. Alexander, A. A. Stevens, C. M. Cabot.

G. E. LEARMONTH

The Montreal Medico-Chirurgical Society

The twelfth regular meeting for the season of the Montreal Medico-Chirurgical Society was held at the Children's Memorial Hospital on May 7th. The usual interesting and varied collection of clinical, pathological and x-ray material was exhibited by the staff of the hospital. After this an address was given by Dr. H. B. Cushing on a subject of unusual importance, namely "The risks of transmission of disease in blood transfusion". Dr. Cushing first dwelt on the great extent to which blood transfusion is now practised in all hospitals. Where five years ago there might have been only a few transfusions in this hospital there were now an average of over 300 per year. The value of blood transfusion was undoubted in such conditions as marasmus and malnutrition, hæmorrhage, hæmorrhagic diseases, anæmia, and certain toxæmias such as those following burns. In passing, he had a word to say about the tendency of some surgeons to use transfusion in acute infections, but with this practice he was not in sympathy as he did not believe that the results were beneficial.

There was no doubt that the technique of blood transfusion had become perfected to a point at which the risk of the procedure was practically nil; the apparatus had been improved, and our methods of blood matching were completely well understood. In spite of all this, however, Dr. Cushing pointed out, transfusion was attended by certain very serious possibilities, the chief of which he had set down as his subject for discussion. Certain diseases stood out as being more likely to be

transmitted in this way, and the chief of these was unquestionably syphilis. The literature showed a number of cases in which this transmission had occurred beyond any question, and it could not be denied that the risk was still a very great one. The precaution was always taken to test the donor for syphilis, but unfortunately the ordinary Wassermann test could not be accepted as an absolute guarantee in all cases. For example, the disease might be contracted after the test had been performed. He reminded his audience that by law a hospital was held responsible if this disease was transmitted to a patient by transfusion, on the ground that insufficient precautions had been taken. In the Children's Memorial Hospital he had established the procedure that in addition to the Wassermann test the blood of all donors should undergo the Kline test which was a great deal more delicate and reliable in proving that the donor was free of syphilis.

Next to this disease perhaps in frequency of transmission was malaria. Its chronicity was well recognized, and apparently it was quite possible to transmit it a great many years after there had been no clinical signs. He spoke, of course, only of donors who were afebrile. Naturally no donor would be accepted who showed any fever whatever. In the Children's Memorial Hospital there were records of four children who had unwittingly received malarial infection through transfusion of blood from their parents. These were all of foreign extraction, but in each case the donor had been for a considerable period in Canada, one of them as long as 35 years. Fortunately this was a disease which could easily be controlled as soon as it was recognized. Typhoid was another chronic disease which it was quite within reason to expect might be transmitted from time to time but he had had no experience in the children's wards of such transmission.

A brief reference was made to the possibility of transmitting allergic conditions by transfusion. Several cases were on record, and he recalled in particular the one in which a woman who was sensitive to gin in the form of intense urticaria, received a transfusion from a donor who, in order to fortify his courage had immediately beforehand taken a large drink of gin, with the result that the receptor developed an intense attack of urticaria after the transfusion.

Dr. Cushing closed his remarks by dwelling on the extreme importance of the question, particularly with regard to transmission of syphilis. In the discussion that followed, Professor E. G. D. Murray pointed out that the incubation period of diseases was something of which we had very little accurate knowledge and yet it was during that period that the risk dealt with by Dr. Cushing was at its greatest. Unquestionably the blood might contain large quantities of pathogenic organisms without any clinical signs or symptoms whatever.

The Regina and District Medical Society

The annual meeting of the Regina and District Medical Society was held at the Hotel Saskatchewan. After a dinner meeting the following officers were elected: *Honorary President,* Dr. C. M. Henry; *President,* Dr. W. A. Thompson; *First Vice-president,* Dr. L. Roy; *Second Vice-president,* Dr. E. A. McCusker; *Secretary,* Dr. S. Larson; *Treasurer,* Dr. H. Spooner; *Executive,* Drs. D. W. Johnstone, D. S. Hart, A. C. MacMillan and J. L. Brown.

The Saint John Medical Society

The annual meeting of the Saint John Medical Society was held as usual at the Byng Boys Club in Saint John, and took the form of a banquet, presided over by the first vice-president, Dr. R. T. Hayes, in the absence of Dr. F. C. Jennings, who was unable to attend. The work of the year was reviewed and the outgoing officers were complimented for their exceptionally good programs carried on during the winter months. Election of officers for 1937 and 1938 resulted as follows: *President,* Dr. R. T. Hayes; *Vice-president,* Dr. V. A. Snow, of Hampton; *Treasurer,* Dr. Gilbert B. Peat; *Secretary,* Dr. Wm. J. Baxter.

The Winnipeg Medical Society

The annual meeting of the Winnipeg Medical Society was held on May 14th. The election of officers resulted as follows: *President,* Dr. O. J. Day; *Vice-president,* Dr. H. D. Kitchen; *Treasurer,* Dr. C. M. Strong; *Secretary,* Dr. R. W. Richardson; *Trustee,* Dr. A. R. Winram.

The retiring President, Dr. W. E. Campbell, gave the presidential address, in which he opposed any regimentation of physicians.

ROSS MITCHELL

Post-Graduate Courses

Annual Refresher Course at the University of Western Ontario Medical School

The University of Western Ontario, London, wishes to direct attention to the Refresher Course which will be given in September, as follows.

Monday, September 13th
- 9.00 a.m. to 11.00 a.m. —Surgery.
- 11.00 a.m. to 12.00 noon—Eye, Ear, Nose and Throat.

Tuesday, September 14th
- 9.00 a.m. to 11.00 a.m. —Medicine.
- 11.00 a.m. to 12.00 noon—Clinical Laboratory Methods.

Wednesday, September 15th

9.00 a.m. to 11.00 a.m. —Obstetrics and Gynæcology.
11.00 a.m. to 12.00 noon—Clinical-Pathological.

Thursday, September 16th

9.00 a.m. to 11.00 a.m. —Pædiatrics.
11.00 a.m. to 12.00 noon—Obstetrics.

Friday, September 17th

9.00 a.m. to 10.30 a.m. —Medicine.
10.30 a.m. to 12.00 noon—Surgery.

Radiology to be included in one surgical period.

Detailed programs will be mailed upon request to all who are interested. Address inquiries to: The Dean, University of Western Ontario Medical School, London, Ontario.

Children's Memorial Hospital, Montreal

PROGRAM

MONDAY, SEPTEMBER 13, 1937

9.30 a.m.—Acute anterior poliomyelitis, Dr. H. B. Cushing.
10.30 a.m.—After treatment of poliomyelitis, Dr. J. G. Shannon.
11.30 a.m.—X-ray demonstration of pulmonary conditions in infancy and childhood, Dr. A. E. Childe.
2.00 p.m.—Acute and chronic otitic conditions common to early childhood, Dr. K. O. Hutchison.
3.00 p.m.—Infant feeding, Dr. A. Goldbloom.

TUESDAY, SEPTEMBER 14, 1937

9.30 a.m.—Burns, Dr. R. R. Fitzgerald.
10.30 a.m.—Pneumonia in children, Dr. L. M. Lindsay.
11.30 a.m.—Common skin diseases, Dr. J. F. Burgess.
2.00 p.m.—Common types of fractures in childhood, Dr. D. E. Ross.
3.00 p.m.—Non-cardiac manifestations of rheumatic disease, Dr. R. R. Struthers.
4.00 p.m.—Thymus gland in infancy, Dr. G. Ross.

WEDNESDAY, SEPTEMBER 15, 1937

9.30 a.m.—Rheumatic cardiac disease, Dr. S. J. Usher.
10.30 a.m.—Origin and pathology of masses in the necks of infants and children, Dr. L. J. Rhea.
11.30 a.m.—Urinary infections in childhood, Dr. D. MacKenzie.
2.00 p.m.—Allergy in childhood, Dr. H. L. Bacal.
3.00 p.m.—Childhood tuberculosis, Dr. P. N. MacDermot.
4.00 p.m.—Metabolism Department — Nephritis and nephrosis, Dr. A. Ross.

THURSDAY, SEPTEMBER 16, 1937

9.30 a.m.—Differential diagnosis of vomiting, Dr. A. Goldbloom.
10.30 a.m.—Treatment of congenital deformities, Dr. N. T. Williamson.
11.30 a.m.—Acute and chronic abdominal conditions, Dr. R. R. Fitzgerald.
2.00 p.m.—Eye diseases met with in general practice, Dr. H. S. McKee.
3.00 p.m.—Empyema, lung abscess and bronchiectasis, Dr. D. E. Ross.

FRIDAY, SEPTEMBER 17, 1937

9.30 a.m.—Acute and chronic osteomyelitis, Dr. R. R. Fitzgerald.
10.30 a.m.—Alimentary toxicosis, Dr. L. M. Lindsay.
11.30 a.m.—Nutritional and deficiency diseases, Dr. H. B. Cushing.
2.00 p.m.—Acute intestinal obstruction, Dr. D. Ross.
3.00 p.m.—Pathology of tuberculosis in children, Dr. F. W. Wiglesworth.

SATURDAY, SEPTEMBER 18, 1937

9.30 a.m.—Diagnosis and treatment of congenital syphilis, Dr. H. S. Mitchell.
10.30 a.m.—Epilepsy and convulsions, Dr. H. M. Keith.
11.30 a.m.—Discussion and demonstration of anæsthesia in children, Dr. W. Bourne.

Clinical meeting: Friday evening, September 17, 1937. Saturday afternoon—golf. Dinner at the Faculty Club, Thursday evening, September 16, 1937. Each lecture will last 45 minutes, followed by 15 minutes for discussion. Special demonstrations will be arranged in tonsillectomy, blood transfusions, other intravenous therapy, and surgical technique for small groups, if desired.

Applications for the course will be received by Dr. J. E. DeBelle, Superintendent, Children's Memorial Hospital, Montreal. Fee for the course $15.00, to be remitted with application.

1937 Graduate Fortnight of the New York Academy of Medicine

The Tenth Annual Graduate Fortnight will be held November 1 to 12 and will be devoted to a consideration of Medical and Surgical Disorders of the Urinary Tract. The subject will include Bright's disease, arterial hypertension, and infections, tumours, calculi and obstructions of the urinary tract, and will exclude venereal disease, diseases of the genitalia and gynæcology.

Twenty important hospitals of the city will present co-ordinated morning and afternoon clinics and clinical demonstrations. At the evening meetings prominent clinicians of New

York and many of the other leading medical centres of this country who are recognized authorities in their special fields will discuss the several aspects of the general subject.

A comprehensive exhibit of books, pathological and research material, diagnosis, treatment and prevention whenever possible, clinical and laboratory diagnostic methods, x-rays, action of drugs and other therapeutic measures. Demonstrations will be held at regular intervals.

Some of the features to be presented at the meetings, in the clinics and in the exhibit will be:—

Physiology of the kidney.
Tests for kidney function.
Œdema and its treatment.
Uræmia and pathology of kidney function.
Pathology of nephritis.
Clinical aspects of nephritis including glomerular, focal, embolic and acute interstitial nephritis.
Nature of hypertension.
Clinical aspects of hypertension, including malignant hypertension.
Evaluation of the surgical treatment of hypertension.
The nephroses.
Vascular and renal complications of pregnancy.
The relation of psychogenic factors of hypertension.
Pathogenesis and treatment of renal infections.
Renal and perirenal infections.
Tuberculosis of the kidney.
Calculous disease. The formation of stones.
Clinical aspects of calculus disease.
Hydronephrosis and pyonephrosis.
Bright's disease in children.
Common urological diseases in children.
Radiotherapy of tumours of the urinary tract.
Tumours of the kidney and ureter.
Tumours of the urinary bladder.
Pathological physiology of bladder-neck obstructions.
Transurethral resection of bladder-neck obstructions.
Surgical treatment of obstructions at the neck of the bladder.

The medical profession is invited to attend. A complete program and registration blank may be secured by addressing Dr. Mahlon Ashford, the New York Academy of Medicine, 2 East 103rd Street, New York City.

University Notes

University of Alberta

Thirty-two physicians graduated from the University of Alberta this year. Few of these are going into practice at once; nearly all are taking the examinations of the Dominion Medical Council.

The following won the five scholarships offered by the College of Physicians and Surgeons of Alberta: final year, medicine, Ronald Hilborn Horner; final year, surgery, Gurth Daniel O'Brien; second year proficiency, Constant Megas; second and third year anatomy, Anthalie Winnifred Heath; third and fourth year physiology, Milton Share.

McGill University

At the May Convocation of McGill University 103 candidates received the M.D., C.M. degree. The following are the prize-winners: The Holmes Gold Medal for the highest aggregate in all subjects forming the medical curriculum, and the J. Francis Williams Fellowship in Medicine and Clinical Medicine; fourth place aggregate standing in the final year, G. Meiklejohn, Berkeley, Calif. The Wood Gold Medal for the best clinical examinations in the subjects of the final year; third place aggregate standing, J. B. Feltner, Stuyvesant Falls, N.Y. The Lieutenant-Governor's Silver Medal for the highest standing in Public Health and Preventive Medicine and Jeanie Forsyth Prize for high standing in Surgery, first place aggregate standing, C. H. Crosby, Melville, Sask. The Alexander D. Stewart prize for the highest general qualifications for the Practice of Medicine, tenth place aggregate standing, H. L. Trimingham, Montreal.

The University of Manitoba

At the convocation of the University of Manitoba on May 19th 52 students received the M.D. degree. John A. Hillsman, Jr., M.D. (Virginia) and John McFaul McEachern, M.D. (Toronto) received the degree of Doctor of Medicine *ad eundem gradum*. Stanley Gordon Herbert, M.D., received the degree of Master of Surgery.

The University Gold Medal in Medicine was won by Gerda Elisabeth Fremming, who also won the Manitoba Medical Association Gold Medal for highest standing in the first four years of the course and the Chown Prize in Surgery, Gold Medal, and $50.00. Robert Inglis won the Dr. Charlotte W. Ross Gold Medal for highest standing in Obstetrics during the course, and Joseph Robert Campbell the Chown Prize in Medicine, Gold Medal, and $50.00.

University of Toronto

Medals, prizes, scholarships and fellowships awarded by the Senate of the University, Faculty of Medicine.

Sixth year.—The Faculty Gold medal, K. J. R. Wightman; the Faculty Silver Medal, W. L. M. King; the Faculty Silver Medal, A. W. Bagnall, B.A.; The Ellen Mickle Fellowship, K. J. R. Wightman; the Chappell Prize in Clinical Surgery, H. Hayward; the William John Hendry Memorial Scholarship in Obstetrics and Gynæcology, J. D. Markham; the Ontario Medical Association Prize in Preventive Medicine, D. G. H. MacDonald; the Canadian Medical Institute Prize, H. C. Balmer.

Undergraduate.—The David Dunlap Scholarships: (*a*) fifth year, A. Auerback; (*b*) third year, J. H. Tritt; the Ronald S. Saddington

Medal in Pathology, D. H. Copp, B.A.; the Toronto Women's League of the United Synagogue, G. A. Lane; the Baptie Scholarship, J. G. Mickler.

Graduate.—The Reeve Prize, G. E. Hall, N.S.A., M.A. M.D., Ph.D.; the Starr Gold Medal, W. L. Donohue, M.A., M.D.; the Alexander McPhedran Research Fellowship in Clinical Medicine, R. C. Dickson, M.D.; the Perry Goldsmith Prize in Oto-laryngology, P. E. Ireland, M.D.; the Faulkner Medal in Psychiatry, G. E. Hobbs, B.A., M.D., D.Psych.; the George Armstrong Peters Prize, C. H. Watson, M.B.; the J. J. Mackenzie Fellowship in Pathology and Bacteriology, H. C. Hair, M.D.

The University of Western Ontario

At the convocation held on June 2nd the degree of M.D. was conferred on 46 candidates.

Prizes and scholarships were awarded as follows: The Alpha Kappa Kappa Gold Medal, Mary M. Wong. The J. B. Campbell Memorial Scholarships, (*a*) Medicine, W. R. Webster, (*b*) Physiology, E. L. Brown. The Roche Scholarship, W. E. Gibson. The Khaki University and Y.M.C.A. Scholarship, H. N. Elliott. The W. H. McGuffin Scholarship in Radiology, M. W. Stapleton. The Rowntree Prizes in Medical History, 1st, B. L. Hession; 2nd, J. G. Stapleton; 3rd, M. W. Stapleton. The Ontario Medical Association Scholarship, E. L. Barton and E. L. R. Schram. Prize in Psychiatry donated by Dr. B. T. McGhie, Deputy Minister of Hospitals, W. J. Tighe. The Essex County Alumni Prize in Obstetrics, J. D. Munn.

Letters, Notes and Queries

Von's Pink Tablets

To the Editor:

Could you tell me anything concerning the ingredients of Von's Pink Tablets?

Yours very truly,

W. E. HUME.

Sherbrooke, Que.,
May 10, 1937.

Answer:—

The Bureau of Investigation of the American Medical Association, to which we referred this enquiry, replies as follows.

" 'Von's Pink Tablets' are sold by a concern that has branches in numerous cities of the United States. There is a New York Von Company, a Cleveland Von Company, an Omaha Von Company, etc. A seizure was made of the Von's Pink Tablets put out by the Omaha branch late in 1932, and the stuff declared misbranded under the National Food and Drugs Act. The government chemists who analyzed the tablets in this connection reported that they were essentially bismuth subnitrate, magnesium oxide and sodium bicarbonate. This composition is rather typical of the stomach tablets that have flooded the market in recent years and have been exploited chiefly through radio ballyhoo.

"In June, 1933, the Federal Trade Commission at Washington announced that George Von Nieda, trading as the Von Drug Company, Minneapolis, Minn.—vendor-advertiser of 'Von's Stomach Treatment' and 'Von's Pink Tablets'—had agreed to discontinue the use of the word 'heal', 'cure' or 'rid' in connection with his stomach-ulcer treatment, and also agreed that in all future advertising this stomach-ulcer treatment should be referred to as relieving hyperacidity or excess acid in the stomach."

Answers to letters appearing in this column should be sent to the Editor, 3640 University Street, Montreal.

Burdock Blood Bitters

To the Editor:

Could you please supply me with an analysis of the patent medicine Burdock's Blood Bitters, or advise me where I can get the information?

Yours truly,

J. D. GRANDY.

Loon Lake, Sask.
May 10, 1937.

Answer: —

We referred this question to the Bureau of Investigation of the American Medical Association, which kindly replies as follows.

"The only information we have about 'Burdock Blood Bitters' was given in the 1914 Report of the Connecticut Agricultural Experiment Station, as follows:

> "This 'safe' remedy contains over 19 per cent of alcohol, with only 4.85 per cent of solids (nearly half of which is sugar), and alkaloids possibly derived from hydrastis. The amount of vegetable extractives is small, certainly not enough to give the results claimed.

"From the composition reported, and also from the name of the stuff, it appears to be one of the nostrums of the old 'blood purifier' type. Such products, as you know, are useless, as they do not purify the blood."

Topics of Current Interest

Radium from Canada

The isolation of radium from the streak of silver-radium ore near the Great Bear Lake has been progressing rather rapidly. From an official statement recently issued by the Eldorado Gold Mines, Ltd., who mine, carry, and refine the pitchblende, it seems that unusual problems were posed by the unparalleled richness of the ore in radium. The technical side of production has now been solved by the Department of Mines with the assistance of Mr. L. Pochon, who had worked at the Curie laboratories in Paris. By October, 1936, the production of radium had reached two grams monthly, and the first ounce was completed on November 16th. The capacity of the refinery is expected to be trebled shortly, and orders to the value of more than £800,000 are to be met in the coming year. It is stated that the market price of radium has been halved as a result of developments in Canada, and there is welcome announcement that with increasing success there is no intention of raising the Canadian price to an exorbitant level.—*The Lancet*, 1937, **1**: 217.

The Sanitary Value of Sodium Metaphosphate in Mechanical Dish-washing

According to a recently completed investigation of the Mellon Institute, the utilization of sodium metaphosphate represents an important contribution to both æsthetic and sanitational progress in machine dish-washing. The results of a bacteriological study of dishes washed in restaurants under routine operating conditions indicate the superior sanitary quality of dishes cleaned with an alkaline detergent containing sodium metaphosphate. This superiority is not attributable to the germicidal action of sodium metaphosphate but to its specific function in preventing the deposition of films of insoluble alkaline-earth salts and soaps. Film formation in dish-washing is a source of great concern to health and restaurant officials because such films form an ideal environment for bacterial growth. The utilization of the film-preventive function of sodium metaphosphate constitutes a novel and significant improvement in dish-washing sanitation. Copies of the research report are available from Mellon Institute, Pittsburgh, Pa.

A Cut in Income Tax Proposed

A novel plan for the reduction of income taxes now paid by people in the middle class is proposed by the Health Guild of America in an article appearing in the May issue of *Health Digest*.

In brief, the plan proposes that, since the cost of government is borne chiefly by the taxes raised on incomes, the tax payer should be permitted to deduct from his gross income any sums expended in the cause of health. This would make it possible for a man to deduct his doctors' bills, dentists' bills, and hospital expenses from his gross income.

The Health Guild argues that such expenditures rightfully come under the heading "cost of doing business" and therefore should be permissible deductions. The Guild further suggests legislative action to amend the present income-tax laws.

If the proposal is accepted by the Senate, it may happen that doctors' bills will be the first paid instead of the last paid, as they proverbially are.

Abstracts from Current Literature

Medicine

Diagnosis of Diseases of the Stomach by Gastroscopy and X-ray Relief Studies. Schloss, J., Ettinger, A and Pratt, J. H.: *Am. J. M. Sc.*, 1937, **193**: 171.

Advances in technique and improvements in the gastroscope are responsible for the widespread use of gastroscopy in the diagnosis of lesions of the stomach. This procedure, in conjunction with x-ray studies, now offers a means of arriving at a correct diagnosis in a high proportion of heretofore obscure cases.

The modern gastroscope differs from its predecessors in having a flexible lower half permitting a wide range of movement. It contains a complicated system of lenses of short focal distance whereby the operator is permitted to view objects or surfaces in proximity to it. The diameter of the tube is only 7.3 mm. The instrument can therefore be operated with a minimum of discomfort and danger to the patient.

Combined x-ray and gastroscopic studies have been made by the authors on 100 consecutive cases. By this method of study it was possible to demonstrate chronic gastritis, gastric ulcer, and even gastric carcinoma in cases where the lesions were unsuspected by clinical and x-ray methods alone. Thus in 19 cases where the clinical diagnosis was normal stomach or gastric neurosis the following results were obtained: (*a*) x-ray examination—normal 12 cases, (gastritis 5 cases, gastric ulcer no cases, carcinoma 1 case, and atrophy 1 case); (*b*) by gastroscopy the diagnosis in these cases was normal 7 cases, gastritis 8 cases, gastric ulcer 3 cases, carcinoma 1 case. In the 100 cases studied the x-ray examination revealed lesions in only 40 cases,

whereas gastroscopy showed gastric changes in 62. Erosions and atrophy of the stomach mucosa can be diagnosed as a rule by gastroscopy only.

The authors feel that the x-ray relief study method and gastroscopy supplement one another in an almost ideal way. The combined methods are to be commended particularly in the demonstration of gastric ulcers, stomach tumours and post-operative pathological changes.

E. S. MILLS

The Clinical Diagnosis of Polyarteritis Nodosa. Leishman, A. W. D., *The Lancet,* 1937, **14**: 803.

During seventy years of its recognized existence about 200 cases of polyarteritis nodosa have been reported, and in only 30 of these cases has the diagnosis been made during life, usually by an exploratory laparotomy or biopsy of cutaneous lesions, although in a small group it has been made on clinical grounds alone. The author attempts an analytical clinical survey of these cases with a resynthesis which might serve as a foundation for the clinical diagnosis of the condition. The historical, pathological, and etiological aspects are briefly discussed and fifteen fundamental signs of diagnostic value in their order of frequency of occurrence are listed as follows: fever, increasing general weakness, albuminuria, cylindruria, leucocytosis, anæmia, tachycardia, abdominal symptoms, polyneuritis, polymyositis, œdema, cutaneous lesions, cardiac signs, enlargement of the liver, and respiratory symptoms. The basic clinical picture is that of a severe progressive toxæmia characterized by fever, muscular asthenia, loss of weight, and anæmia; the course is usually, but not always, fatal. The author cites 4 cases which have occurred in three years in St. Bartholomew's Hospital, and concludes with the suggestion that through a better understanding of the clinical picture as outlined the diagnosis may be made ante mortem.

DAVID RODGER

Surgery

Early Local Care of Face Injuries. Blair, V. P., Brown, J. B. and Byars, L. T., *Surg., Gyn. & Obst.,* 1937, **64**: 358.

Early proper care of the injuries of the face is as important cosmetically as early care of the emergent surgical abdomen is vitally. The bony structure of the face is the framework for reconstructive measures. Wiring of the teeth in upper and lower jaw fractures, instigated and popularized by the late Thomas Gilmer, has shown the principle upon which all the bones of the face may be retained. Lack of usable teeth does not prevent the use of wire in the retention of displaced fragments of the upper and lower jaws. Backward displacement of the chin fragment in a double fracture of the body of the mandible is best treated by an open-bite splint (Gunning type). Most fractures of the upper and lower jaws can be satisfactorily treated by simple wiring of the lower and upper teeth. Twenty-four-gauge soft brass wire is the most satisfactory. Fractures of the palate are readily replaced by pressure in the floor of the nostrils. In all but the upper loculate fractures (through the orbits, nasal cavity and pterygoid processes) which should be left 7 to 10 days before replacement because of the advisability of drainage, reduction and fixation should be performed at once and maintained for 3 weeks. Most malar displacements can be replaced by a long, slender bone elevator, inserted at the upper part of the temporal ridge, prying the bone into position. The common (usual) backwards displacements of the frontal process of the maxilla and of the nasal bones can be reposed through the nasal cavity. Mesial compression by lion-toothed forceps assists in lateral displacement of the lachrymal bones. It is a moot question whether vaseline-coated nasal packing is of retentive value. Nasal bones are best held in position by an adjustable intranasal attachment to a dental splint. Lateral displacement of nasal cartilages should be replaced immediately, and if necessary sutured and fixed to the teeth on the uninjured side. The familiar "trap-door" flap should be thoroughly cleansed and sutured with triple 0 white silk interrupted, being subdermal on the flap side to the deeper part of the derma on the opposite side, with another layer of sutures to the skin with slight overlapping from the flap side, or a few "tacking" sutures allowing drainage should be applied. A rubber-band drain should be used for 24 hours. An elastic compression bandage is essential. Any break in cartilage should be sutured by fine silk. All imbedded foreign particles should be removed at primary suture. Oil "tattoo" marks may have to be treated by secondary full thickness skin grafts. Throughout, subcuticular suture with fine silk with adhesive plaster skin coaptation is much favoured.

FRANK DORRANCE

Obstetrics and Gynæcology

The Endometrial Theory of Ectopic Pregnancy. Frankel, J. M. and Schenck, S. B., *Am. J. Obst. & Gyn.,* 1937, **33**: 393.

All ectopic pregnancies, tubal or otherwise, occur because of nidation of the fertilized ovum in a locus of ectopic endometrial tissue to which the ovum is chemotactically attracted. The fate of the gestation depends upon the amount of endometrial tissue to undergo the decidual reaction and upon the depth of penetration of the ovum beyond the borders of this decidua. All ectopic pregnancies are primary.

ROSS MITCHELL

Oral Paraldehyde Administration in Obstetrics. Douglass, L. H. and Peyton, F. W., *Am. J. Obst. & Gyn.*, 1937, **33**: 604.

To mask the disagreeable odour and to make the preparation palatable, the paraldehyde was mixed with propylene glycol, alcohol and syrup of acacia. A dose of five drams of paraldehyde was found most satisfactory for oral administration. The absorption time was rapid. Memory disappeared five to ten minutes after the preparation was swallowed. Complete amnesia was present in 94 per cent of the fifty cases. No deleterious effects to either mother or infant were noted. A more complete study is under way. ROSS MITCHELL

The Incidence of Ureteral Stricture in Lower Abdominal Pain in Women. Lintgen, C., *Am. J. Obst. & Gyn.*, 1937, **33**: 636.

In a series of 136 having lower abdominal pain 26 patients were shown to have ureteral strictures. In women who had borne children the obstruction was from 3 to 6 cm. above the ureteral orifice in every instance, while in the non-gravid group the obstruction was higher up in 75 per cent of the cases. Ureteral stricture should be considered as a possible diagnosis in all cases of chronic lower abdominal pain in women. ROSS MITCHELL

Congenital Atresia of the Œsophagus with Tracheo-Œsophageal Fistula (3 Cases). Rosental, A. H., *Am. J. Obst. & Gyn.*, 1937, **33**: 646.

Three cases of congenital atresia of the œsophagus with tracheo-œsophageal fistula have occurred within a period of two years on an obstetric service where 1,200 women are delivered yearly. It is probable that many cases escape true diagnosis. The obstetrician often has the opportunity of observing the first clinical sign of the malformation, namely, the presence of a large amount of mucus in the mouth and pharynx of the newborn, and difficulty in clearing the respiratory passages by aspiration. The most characteristic symptom is the regurgitation that occurs after each feeding, often accompanied by coughing and cyanosis. The diagnosis can be easily confirmed by the passage of a catheter into the œsophagus and roentgen visualization after the introduction of a radio-opaque fluid. ROSS MITCHELL

Pædiatrics

Acute Appendicitis in the Exanthems. Bullowa, J. G. M., McCabe, E. J. and Wishik, S. M., *Am. J. Dis. Children*, 1937, **53**: 1029.

These authors call attention to the fact that vomiting and abdominal pain are common at the onset of eruptive fevers. Ordinarily, these signs subside and the disease takes its normal course. There are, however, exceptional cases in which surgical intervention is called for. It is important to remember that such a situation may arise.

In 26,462 patients treated at the Willard Parker Hospital, New York, appendicitis occurred 21 times. The incidence for the various diseases was as follows:

Disease	*No. of cases*	*No. of cases of appendicitis*	*Percentage*
Measles	6,357	11	0.17
Varicella	2,534	5	0.19
Scarlet fever	6,252	3	0.04
Diphtheria	4,140	0	
Pertussis	1,219	0	
Other diseases	5,960	2	0.03

During the prodromal period of measles acute appendicitis is very unusual; in the eruptive period it is most rare, and early perforation and extensive tissue necrosis are the rule. The appendicitis is not usually recognized before perforation has occurred because the physician's attention is focused on the respiratory and cutaneous features of the measles. The authors urge that abdominal symptoms occurring in the exanthems, especially in measles and varicella, should receive special attention, in as much as they may be due to acute appendicitis. JOHN NICHOLLS

The Iron-Deficiency Anæmia of Late Infancy. Fullerton, H. W., *Arch. of Dis. in Childh.*, 1937, **12**: 91.

This is a study of the anæmias in 789 infants in Aberdeen, Scotland, of all ages up to 23 months. Subnormal levels for hæmoglobin (less than 80 per cent—Haldane) were found in 87 per cent of 298 poor-class infants between the ages of 9 and 23 months. The common anæmia of infancy is due mainly to deficiency of iron, and this in turn is dependent on low birth-weight, artificial feeding, and infective illness, and not to any extent on a deficiency of iron in the mothers. The incidence of anæmia among the children of the better classes is probably less than among the poor, but yet, is of real importance. The author does not think that the dietary regimen commonly in use should be altered by the introduction of foods rich in iron in larger quantity and at an early age unless the pædiatrician decide that this should be done. Medicinal iron is well borne by children, and should be given routinely at the age of three months to all infants who weighed less than seven pounds at birth, in cases or artificial feeding, and after illnesses of an infective nature. In the last event treatment should be continued for at least two or three months. A caution is given as to the difficulty of correctly diagnosing anæmia in infancy in the absence of a hæmoglobin estimation, for appearances are deceitful. Infants who are regularly placed in sunshine and fresh air often look well and yet are anæmic. JOHN NICHOLLS

Studies of Latent Scurvy in Infants: I. Capillary Resistance of Newly Born Children and During the First Year of Life. Bræstrup, P. W., *Acta Pædiatrica,* 1937, **19**: 320.

On the basis of 400 determinations of the capillary resistance in normal children under one year of age, Bræstrup found that newly born children have an extraordinary capillary resistance by stasis-test during their first five days, regardless as to whether they are prematurely born; that the resistance of about half the healthy children aged one to five months and fed exclusively on mother's milk is lowered; that the capillary resistance of about 10 per cent of children from six to twelve months old, on a mixed diet, is lowered.

Ascorbic (cevitamic) acid was administered to 8 diseased children, whereupon the resistance of 3 became normal. The lowered capillary resistance of 6 out of 10 healthy children became normal after the administration of tomato juice. The author concludes that a common cause of lowered capillary resistance in otherwise healthy infants is too little vitamin C.

JOHN NICHOLLS

Ophthalmology

Research on Lachrymal Elimination of Sodium Chloride. Michail, D., *Ann. d'Ocul.,* 1936, **173**: 715.

Numerous studies have been made on the function of the lachrymal apparatus, but they have not up to the present made clear important physiological questions. In the course of his researches the author has attempted to determine the percentage of sodium chloride in tears in normal and pathological conditions.

The mean rate of lachrymal elimination of NaCl for normal eyes is 8.23 0/00. Acute affections of the eyes lower the lachrymal elimination of NaCl, while chronic affections raise it. This constitutes one of the most expressive facts in pathological lachrymal function. The variations which the lachrymal elimination of NaCl manifests under the influence of pilocarpine, lachrymal gland extract, oculo-cardiac reflex, show that this lachrymal function is in relation with the lachrymal neuro-vegetative apparatus. Sympathetic excitation provokes elevation, and excitation provokes lowering of the rate of lachrymal elimination of NaCl. The ovarian hormone causing elevation of the elimination rate shows itself as a sympathicotone substance. Its action affects both sexes, but shows up particularly in the female during the period of sexual activity.

Injections of solutions of NaCl provoke lachrymal sympathicotone effects when they are given around the ocular region, and amphotone when they are given in facial regions away from the eyes. Intramuscular injections of milk react simultaneously and in the same manner on the thermogenesis and lachrymal elimination of NaCl, but the action may be a little more prolonged on the last element. Peri-carotid sympathectomy provokes a lowering of the lachrymal elimination rate, which shows in an experimental manner the influence of the neuro-vegetative system on the lachrymal function.

S. HANFORD MCKEE

A Note on Expulsive Hæmorrhage. Averbach, M., *Ann. d'Ocul.,* 1937, **174**: 44.

This is one of the gravest maladies of the eye, or rather one of the graver complications of certain ocular affections. All practitioners have had occasion to observe this clinical condition in one form or another. The author recalls a patient suffering from absolute glaucoma of the eye, complicated by attacks of keratitis, and where later erosion of the cornea occurred, followed by an expulsive hæmorrhage for which the patient was brought to hospital. As it was impossible to relieve the pain the eye was enucleated.

Where does the blood come from in expulsive hæmorrhage? The author believes that it originates behind the choroid, that is to say, in the supra-choroidal space. From this hypothesis he concludes that as the blood comes from the supra-choroidal space and does not meet with any obstacles in the sclera, with an opening there, it would discharge without provoking an expulsive hæmorrhage. For this reason the dissection of a triangular valve in the sclera has been suggested. The details of a number of cases are given.

S. HANFORD MCKEE

Urology

Transurethral Resection: its Indications, Limitations and Complications. Bumpus, H. C., *Surg., Gyn. & Obst.,* 1937, **77**: 324.

The author, a pioneer in this work, believes the factor which constitutes the greatest limitation in this operation is lack of training of the operator and the necessity for him to learn the procedure by trial and error—a wasteful but effective method of learning. In the past the instruments used offered additional limitations, but this is not so with those now on the market. These provide for good and constant visualization with adequate control of bleeding. Large amounts of tissue can be excised, if necessary, to provide free, adequate and unobstructed drainage of the urinary tract—the basic principle of all forms of urinary therapy. To prove his point the author cites figures compiled by Orr which show that the mortality rate following transurethral resection of the prostate bears a direct relationship to the experience of the operator. He believes the best way to evaluate the indications is by the effectiveness of the

procedure in removing obstruction of various degrees to the urinary flow and the risk involved in its accomplishment. He reports figures from the Mayo clinic, from his own practice, and from the clinic of Dr. Alcock which clearly indicate that both small and large prostates can be safely and effectively resected with much less risk to the patient than that involved in the total enucleation of the gland. Lastly, the post-operative complications are discussed. Here again the author believes the chief hazard — hæmorrhage — will be eliminated by special training of the nursing and intern personnel, and their complete familiarity with catheter drainage during the first 48 hours after surgery. To allow the bladder to become distended with blood clot and force infected urine back to the renal pelves may mean the difference between success and failure. The hazard of sepsis will be lessened by the reduction of operative trauma. If sufficient tissue cannot be removed within an hour it is best to discontinue and do further resection after a 4- or 5-day interval.

N. E. BERRY

The Urologic-Orthopædic Viewpoint on the Cord Bladder. Munger, A. D., *J. Urol.*, 1937, **37**: 54.

The ever-increasing frequency of spinal cord injuries demands a well directed procedure in caring for the sequelæ arising therefrom. The author is of the opinion that although the orthopædic and the neuro-surgical attention of the fractured vertebra is without parallel, yet the urological complications, chief among which is the "cord bladder", are often neglected. If the problem was merely that of relief of retention of urine there would be no cause to be concerned, but, as statistical records show us, it is one of urinary tract infections and carries with it a mortality rate of about 40 per cent.

One school of urologists maintains that 75 per cent of the incontinent patients will establish a true automatic bladder in 96 hours, and residual urine and dribbling will cease. The other school, namely, Sir J. Thompson Walker, Alcock, Deming and Davis insist upon immediate suprapubic drainage.

It is apparent that spinal injuries about the 11th dorsal segment stand a better chance of developing automaticity than injury below this level. The author is of the opinion that catheterization should be made a mandatory prohibition; that the patient should be kept comfortable with sedatives for a period of 2 to 4 days with the hope that automaticity may develop. If this method fails or infection supervenes closed suprapubic drainage should be insisted upon at once.

J. V. BERRY

Neurology and Psychiatry

Mental Symptoms in Cases of Sub-tentorial Tumour. Keschner, M., Bender, M. B. and Strauss, I., *Arch. Neurol. & Psychiat.*, 1937, **37**: 1.

Mental symptoms were observed in 47 per cent of the patients with infratentorial tumour, this incidence being half that in a previous series of cases of supratentorial tumour reported by the same authors. Forty-seven per cent is a high incidence when compared with other reports, and is due in part to the very detailed psychiatric examination for slight mental changes which was made on these cases. The mental symptoms were generally mild and not persistent; they appeared usually late in the course of the disease, and as a rule were associated with symptoms and signs of disturbance in function of the cerebellum, brain-stem, and lower cranial nerves. Thirty-five per cent showed disturbances of the sensorium — mild apathy, a tendency to somnolence and lack of attention. Crude visual hallucinations occurred in 4 of the total 120 cases. Twenty-four per cent showed disturbances in affect—euphoria, facetiousness, anxiety, depression, or irritability. There was a low incidence of disturbance of memory, personality and intellect. Disturbances of sphincter control were half as frequent as in the cases of cerebral tumour. In the previously reported groups of supratentorial tumours the mental symptoms were more varied, more severe and persistent; they frequently appeared early in the disease, and were not always associated with the other symptoms of tumour of the brain.

FRANK TURNBULL

The Diagnosis of Chronic Subdural Hæmatoma. Hall, G. S., *J. Neurol. & Psychopathol.*, 1937, **17**: 67.

Basing his premises on a series of 4 cases, the writer emphasizes the importance of this far from infrequent condition. The syndrome presented is variable to a degree, the most striking features being merely those of any increase in intracranial pressure (most commonly headache and papillœdema). These signs of pressure tend to be much less marked in the older patients, a finding attributed to the brain shrinkage of later-age periods. The author does not, curiously enough, stress the very considerable period of time which may elapse before symptoms develop, though this is quite striking in the accompanying case reports.

G. PATERSON-SMYTH

Dermatology

Streptococcic Dermatoses of the Ears. Mitchell, J. H., *J. Am. M. Ass.*, 1937, **108**: 361.

Pruritic and scaling dermatoses of the ears, retroauricular intertrigos with serous crusting, scaling and fissuring, and itching and scaling

of the cavum external meatus and canal are commonly encountered. They are commonly referred to as "eczema" or "seborrhœic dermatitis", and while in Europe for the past thirty years the important rôle of streptococcus in producing these conditions, as indicated by Sabouraud, has been recognized, it is not so regularly accepted in America. Mitchell's clinical and bacteriological experience in these conditions places him in complete accord with Sabouraud's observations. In his paper he presents a series of such cases well illustrated by photographs. Laboratory methods for verifying the diagnosis are given, and the differentiation from similar eruptions sometimes produced by nickel (from spectacle-bows) and other irritants, and by fungi is described. Sabouraud's dictum that streptococci on the skin are never to be considered as saprophytic is emphasized. A critical discussion by a number of members of the American Dermatological Association, before whom the paper was presented, adds much to the value of this paper.

D. E. H. CLEVELAND

Therapeutics

The Therapeutic Use of Venesection in Polycythæmia. Stephens, D. J. and Kaltreider, N. L., *Ann. Int. Med.*, 1937, **10**: 1565.

The syndrome of erythræmia is characterized by a marked hyperplasia of the bone marrow, as a result of which characteristic increases in the red cell count, hæmoglobin, hæmocrit, blood viscosity and blood volume occur. The symptoms of the disease result for the most part from the plethora and stasis of blood flow due to the marked increase in blood volume and overfilling of the capillary bed. Even in those types of polycythæmia in which the increase in red cells seems to be in response to an increase in demand for oxygen-carrying material, the increased blood viscosity may increase the difficulty in oxygen exchange.

The authors studied the effect of venesection in 5 cases of polycythæmia. This was repeated at intervals of from one to several days. It was found possible by withdrawing in all from 1,700 to 3,370 c.c. to reduce the relative volume of the red blood cells to a normal or slightly subnormal level, with a corresponding decrease in the red blood cells and hæmoglobin, and a reduction in the blood viscosity, blood volume and blood velocity to approximately normal levels. This was usually accompanied by a marked relief of symptoms, and by a reduction in the size of the spleen. Nine of the eleven periods of bleeding were followed by no significant increase in the percentage of reticulocytes. In the two cases in which reticulocyte increases occurred the bleeding was done following periods of blood destruction, when the iron stores of the body were excessive. Four of the five patients experienced symptomatic and hæmatological remissions of from eight months to two years' duration without further treatment. This was thought due to the venesection resulting in loss from the body of considerable amounts of iron and other potential blood building materials. Systematic venesection appears to be a relatively safe and efficient therapeutic procedure, which compares most favourably with other measures used in the treatment of polycythæmia.

H. GODFREY BIRD

The Use of Radium in the Treatment of Benign Uterine Bleeding. Malpas, P., *Brit. J. Obst. & Gyn.*, 1937, **44**: 86.

During the past twenty-five years radium has been used more and more in the treatment of benign uterine bleeding. The author believes that radium in the present day finds a greater applicability to the treatment of benign bleeding than of malignant diseases. Four hundred and thirty-two cases of benign bleeding were treated and 200 cases have been followed up. Of these 4 cases were failures. The screening used was 0.5 mm. of platinum, 1.2 mm. of silver and 2 mm. of rubber. The main indications for its use were: (*a*) to produce permanent amenorrhœa; (*b*) for menorrhagia, with conservation of the menstrual function; (*c*) for post-menopausal bleeding.

Eighty-six per cent of the cases followed up manifested permanent amenorrhœa. Five per cent were between 31 and 35 years of age; 8.7 between the ages of 36 and 40; 50 between 41 and 45, 27 between 40 and 50 and 7.5 between 51 and 55. There were no cases of death following operation. There were no cases of post-radial inflammation when it was not present before.

Post-radiated failures fall into the following classifications. (1) Transient return of bleeding after one to two years. Carcinoma of the fundus should be suspected in these cases. (2) Persistent leucorrhœa. In the cases examined by the author persistent leucorrhœa was nil.

Following radium treatment 23 per cent had menopausal flushes, as compared with 46 per cent following surgical castration. It was thought that radium menopause approached more nearly the normal than surgical menopause.

The author refers to the impairment of reproductive power and states references of 600 children born after pre-conceptional maternal irradiation with the average incidence of malformation about 11.6 per thousand. He found it difficult to explain the cause of amenorrhœa, and advances Matthew's theory of persistent corpus luteum tissue, the least susceptible to radiation of all the components of the ovary.

P. J. KEARNS

Pathology and Experimental Medicine

The Bone Marrow in Anæmia. The Red Blood Cells. Isaacs, R., *Am. J. M. Sc.*, 1937, **193**: 181.

Isaacs has studied the development of the red blood cells in the sternal bone marrow of normal persons and patients dead from various diseases which produce anæmia. In some instances the sternal marrow was obtained by biopsy, in others after death from various accidents (normals), or from such diseases as aplastic anæmia, pernicious anæmia, cirrhosis of the liver, hæmorrhage, chronic nephritis, myelophthisic anæmia and infection. A special technique was employed comparable to that used when studying these cells in the peripheral vessels; that is, actual cell counts were made and stained smears studied. He has been able to determine that the distinct morphological stages in the development of red blood cells are (*a*) a primitive blast, (*b*) megaloblast, (*c*) basophilic normoblast, (*d*) eosinophilic normoblast, (*e*) reticulocyte, (*f*) granule red blood cells and (*g*) mature erythrocyte.

In the various pathological stages studied, "block", or arrest of development of the red cells, occurred at different stages of maturition. Thus inhibition of development in the primitive "blast" stage occurred in chronic nephritis and idiopathic aplastic anæmia. Inhibition of development at the megaloblastic stage was found in cases of pernicious anæmia, cirrhosis of the liver, and most macrocytic anæmias. Inhibition delay at the normoblastic stage was evident in cases of leukæmia (myelophthisic anæmia) and in infections associated with anæmia. The author believes that the red blood cells in the bone marrow attain their maximum size in the megaloblast stage while most of the hæmoglobin deposition takes place in the normoblast stage. Delay in development at the megaloblast stage results in large red cells (macrocytes), whereas rapid transition through this stage produces small erythrocytes (microcytes). Further, the shorter time spent in the normoblast stage, the greater the hæmoglobin deficiency of the mature cell. Great difficulty was encountered in drawing conclusions from actual red cell counts from the bone marrow as the physiological variations were found to cover a wide range and changes in response to external requirements took place with great rapidity.

E. S. MILLS

The Effect of Drugs on Different Segments of the Intestine of Man. Guthrie, J. S. and Bargen, J. A., *Surg., Gyn. & Obst.*, 1936, **63**: 743.

In order to obtain readings on kymographic paper, patients with colostomies, of at least 2 weeks' duration were chosen. A thin rubber balloon, 3½ inches in length, was inserted at least 2 inches beyond the inner level of the abdominal wall, and inflated with air to a point short of distension, but filling the entire intestinal lumen. Tracings were obtained from the transverse colon, the sigmoid flexure and a combination of the terminal portion of the ileum and sigmoid flexure after intramuscular injections of pituitrin, physostigmine salicylate, gr. 1/50, peristaltin (Ciba) and acetylcholine, 100, 200 and 400 mg. Pituitrin was found to be the only drug capable of causing a marked peristalsis of both the small and large intestine. It was rapid in its response, consistent in its action, and increased the motility of the intestine without any effect on the tonus. The effects of the other three drugs were of very minor degree and were uncertain and inconsistent.

FRANK DORRANCE

Obituaries

Dr. Ingersoll Olmsted

AN APPRECIATION

I wish to add a few words to the obituary notice of the late Dr. Ingersoll Olmsted, of Hamilton, in the March number of the *Journal*, (p. 323). I knew him from my earliest days for he was devoted to my father, Dr. Archibald E. Malloch, whom he delighted to call his teacher, and he frequently came to our house to talk about patients and to tell a good story. For many years he was a member of the Doctors' Whist Club, (later bridge was played) which met every Wednesday night under my father's roof. Also he very kindly let me assist him at operations during the summer of 1908 before my medical course at McGill began, and between the sessions while it lasted. James K. Bertram, son of Dr. Olmsted's great friend, Dr. T. A. Bertram, of Dundas, had the same privilege, but this promising McGill student was killed during the War before he had finished his medical course.

His skill drew a large number of patients from Hamilton and the surrounding country, and he was one of the ablest surgeons I have known, for the reason that he was much more than a surgeon. Several years of work in bacteriological and pathological laboratories, and years of practice almost entirely limited to medicine, gave him a foundation that comparatively few have had. Whatever he undertook he did with all his might, and did not spare himself; whatever was new in the way of a surgical instrument he would send for, adopt if it helped him in his work, or discard if it proved of little aid. No trip was too long to prevent him going to see a man employ a new method.

He had an x-ray machine and took excellent pictures himself. He quickly adopted local anæsthesia and became expert in its use, even though it had not been employed to nearly the same extent in larger surgical centres. I have known him to employ it for decompression operations and for hernia in his private patients. Dr. Olmsted would do single-handed what elsewhere would require several departments. A patient suffering from symptoms which pointed to the kidney consulted him one day at his office. He x-rayed the kidneys, cystoscoped the patient, catheterized both ureters and stained the urine for tubercle bacilli. Finding them in the urine from one side, he removed the offending tuberculous

kidney the next day, under gas anæsthesia. He was a very dextrous operator—I should say ambidextrous—and it was a delight to see him do a dissection of the neck, or remove a goitre. During the operation he explained to his assistant or to the nurses the why and wherefore of the procedure adopted, and was an excellent, enthusiastic teacher. I can see him now after an operation sketching with a pencil for our benefit exactly what he had done, or showing us with thread and needle and several layers of gauze rolled into a tube, the various stitches he had just employed in the operation of intestinal anastomosis. He was exacting sometimes during operations, but I can remember that on the way home he would stop at a confectioner's shop and order a quart of ice-cream for the benefit of the operating-room nurses.

Dr. Olmsted, owing perhaps to the fact that he had had several severe illnesses himself, could not be outdone by the most skilled nurse in the care of the patient after operation. He knew exactly how pillows should be arranged to bring the greatest comfort and hated to see suffering. Books were literally worn out in lending them to one patient after another (for instance, Ian Maclaren's "Young Barbarians").

His boyhood and youth were spent in the beautiful countryside at Ancaster near Hamilton, and a drive with him to an operation at a farmhouse was a rapid succession of delights as he pointed out the beauties of Nature, an unusual bird, or the first bloom of the season. I have scarcely seen anyone who was fonder of flowers.

From his undergraduate days, Dr. Olmsted was a constant student and he had a good library of medical and surgical works. He was a keen reader of the German and French magazines, many of which he took himself, and I am very glad he advised me to read textbooks in these languages during my medical course and to live in German and French families. Also to keep in practice, he would have a French and German novel on hand.

Dr. Olmsted's energy in work and play was phenomenal and his mind worked like a flash. I must say that a day spent with him was tiring even to a youngster. Before the loss of his leg he was an excellent tennis player; after that, he rode, curled well for years, and played billiards and a good game of golf. For the links at Ancaster he did yeoman service on the Greens Committee. He was an enthusiastic fisherman; so intent on fishing was he that I have known him board a night train at Hamilton for Detroit, solely to purchase a new reel he had heard of. When autumn came round, he always spent several weeks duck-shooting at Big Point on the St. Clair Flats and he was very accurate with his Purdy gun. ARCHIBALD MALLOCH

Dr. Frederick Leslie Beer, of London, Ont., died on May 22, 1937, in his fifty-eighth year.

Dr. Beer was a son of the late Rev. W. C. Beer, a minister in the former Methodist church. He studied medicine at the medical school of the University of Western Ontario (1905) and following his graduation, he practised in Carlyle, Sask., and Brandon, Man., until 1929, when he started practice in London.

Dr. Malcolm McLachlan Crawford, chief coroner for Toronto and supervising coroner for Ontario, died in Toronto on May 14, 1937.

Dr. Crawford was born at Orangeville, Ont., in 1875, the son of Alexander H. and Mary McLachlan Crawford. He was educated at Toronto schools and graduated from the University of Toronto in 1898, taking post-graduate studies at the University of Baltimore. He was associated with the pathological department of the University of Toronto for some time. He interned at St. Michael's Hospital, and was a member of the staff there. For many years he practised on Cumberland Street, later moving to Roxborough. From 1915 to 1920 he served overseas with the Medical Corps.

Dr. R. L. Hurst died in the Winnipeg General Hospital on June 3rd after a protracted illness. He was born at Malverton, Ont., in 1882, graduated in medicine from Toronto University in 1908, studied in London, and practised in Winnipeg from 1912. He is survived by his widow, three sons and one daughter.

Dr. Herbert Maw, of Caledonia, Ont., died suddenly on May 26, 1937. He was born in Georgetown, Halton county, sixty-four years ago, and after graduating from Trinity University, Toronto, in 1897, he practised medicine a few years in eastern Ontario, and came to Middleport thirty-three years ago. Three years later he moved to Caledonia, where he has had a wide practice for thirty years. Although very busy in his chosen profession he found time for work in community affairs and sports. He was local medical officer of health, also Canadian National Railway physician.

Dr. Preston A. M. Lyster, of Castor, Alta., passed away in May in Chula Vista, California, where he went to regain his health. He was born in Kirkdale, Que., but went west as a boy. Prior to the study of medicine he attended Normal School in Calgary in 1914, and taught school in the province. He registered in Alberta in 1924, having graduated from McGill University in 1922.

Dr. Lyster practised in Nordegg, Claresholm and Castor, when he retired on account of ill health; passing away at the age of 48. A man of fine stature, pleasing countenance, cheerful disposition, and thoroughly trained, he was a valuable member of the profession.

Dr. Arthur Mignault, of Montreal, died on April 26, 1937, aged seventy-one. He was a graduate of the University of Montreal (1888).

Dr. Mignault took an active part in the recruiting of French-Canadians for service overseas during the World War, and was instrumental in organizing the 22nd Canadian Battalion, personally offering the sum of $50,000 in September, 1914, toward the expenses of recruiting and training the unit. Later a second French-Canadian unit, the 41st Battalion, was organized as reinforcement for the 22nd, and Dr. Mignault was given the rank of colonel and command of No. 4 Stationary, and three French-Canadian units were in England by May, 1915.

The hospital unit of which Col. Mignault had been given command was only the first of three which he was later to be in charge of, No. 8 General Hospital in Paris, No. 6 General Hospital in St. Cloud, both of the French General Army. For his work overseas Dr. Mignault was made a member of the Legion of Honor.

As late as 1935, Dr. Mignault made an appeal to young French-Canadian doctors to enlist in the British Army, and was responsible for at least two young men taking that step. During the years following the war, he was recognized as an authority on the functioning of the British Army Medical Corps. Only two or three months ago he was elevated to the rank of Brigadier-general.

Dr. Daniel Phelan, of Kingston, Ont., for 20 years surgeon at Portsmouth Penitentiary and a former president of the American Prison Surgeons' Association, died on May 3, 1937. He was recognized as one of America's foremost alienists, but had been retired several years.

Born in North Gower in 1854, Dr. Phelan was educated at Ottawa University and graduated in medicine from Queen's in 1877. He was appointed Portsmouth prison surgeon in 1898.

Dr. David Kenneth Stenton, of St. Thomas, Ont., died on April 12, 1937. He was born in 1859 and a graduate of the University of Western Ontario (1890).

News Items

Great Britain

A Fellowship in Radiology.—It has been evident for some years that radiological diplomas could not be looked upon as more than qualifying examinations, and that it was desirable to give young diplomates something higher to aim at. A new radiological body —the British Association of Radiologists—was founded in 1934, and at once began work on the establishment of a Fellowship. The Association has various activities, but a largely autonomous body, known as the Fellowship Board, was created to deal with matters of Radiological Education. The Board presented its report last year, and a Fellowship Diploma obtainable by examination has been duly established. This examination is open only to those who have held a recognized radiological diploma for at least two years.

The examination differs from the various diploma examinations not only in the standard required but because candidates are to be examined in General Medicine, General Pathology, and in certain aspects of General Surgery. Those responsible for framing the regulations hold that the distinction sometimes made between "clinician" and "radiologist" is fundamentally wrong. They feel that in no special branch of medicine is wide clinical knowledge of more importance than in radiology, and that whatever deficiencies on the clinical side may have existed among radiologists in the past it should not in future be possible to regard their clinical training as less complete than that of their colleagues.

Further information can be obtained from the Warden, Dr. F. Hernaman-Johnson, 32 Welbeck St., London, W.1.

Alberta

While contract practice is on the increase so are the evils attending it. Some blanket contracts made with the profession by municipal districts contain no mileage clause, with the results that frequently doctors' services are not available for needy cases as the doctors are away answering some unimportant calls. This matter was pointed out to several municipalities recently, and now a clause has been added, allowing a mileage fee of 25 cents per mile, with a maximum fee of $4.00 per call, with a minimum of $2.00. Since this went into operation the outside calls have been greatly reduced and the service to those who need has been improved.

During the month of May, 1937, the following District Associations have been having their annual meetings in consecutive order so that the officials of the Provincial Association may attend them: Lethbridge, Medicine Hat, Drumheller, Calgary, Red Deer, Camrose, Edmonton and Northern Alberta.

Dr. Clarence Holmes, who was with the travelling clinic in 1936, heads it this year, with Dr. E. Hitchin as assistant. They are busy at work in the south-eastern portion of the province, where the people have suffered greatly from drought these last few years and the districts are sparsely populated.

The Provincial Association together with the University of Alberta put on a refresher course in Edmonton, May 10 to 14, 1937, which was well attended; over thirty men attending from points outside the city of Edmonton.

The town of Notikewin, 85 miles north-west of the town of Peace River, is to have a church hospital. The building will soon be opened for service. The Women's Missionary Society of the United Church is erecting the building and have engaged a young physician from Eastern Canada to take charge about August 1st. This will be a Godsend to the 3,000 people in the district, who are 65 miles north of the railway line. G. E. LEARMONTH

British Columbia

The Board of Governors have authorized the Vancouver General Hospital to purchase an electric apparatus for producing artificial fever at a cost of $1,054, and to send Dr. Alice J. McDonald, of Vancouver, and another technician to Denver for training in its operation.

The possibility of the Metropolitan Health Board assuming control over venereal disease prevention in Vancouver is being investigated by Dr. J. W. McIntosh, city medical officer. Dr. McIntosh reported to the board at a meeting in the City Hall that he is making progress in his study of the situation. If it appears feasible for the board to undertake the work he will negotiate with the Provincial Government for a grant to cover the program. The latter would include tracing sources and contacts of venereal infection in the city area. D. E. H. CLEVELAND

Manitoba

Under the auspices of the Section of Obstetrics and Gynæcology of the Winnipeg Medical Society two moving picture films,—"Complications of the second stage of labour" and "Eclampsia", were shown in the Physiology Lecture Theatre of the Medical College on May 31st. These films were prepared by Dr. J. B. DeLee, and it was through the kindness of Dr. Sara Pearl, of the staff of the Chicago Lying-in Hospital, that these films were shown. ROSS MITCHELL

New Brunswick

Hon. Dr. W. F. Roberts, Minister of Health for New Brunswick, is at present in the hospital at Montreal, where he has been successfully operated upon.

Dr. A. H. Gordon, of Montreal, was granted an honorary degree of Doctor of Civil Law, at the convocation of Acadia University. Dr. Gordon's friends in the Maritimes join in congratulating a native son who has been honoured by a Maritime university.

Dr. J. A. M. Bell, of Newcastle, is slowly convalescing from a serious illness which has kept him from practice for the last two or three months.

The Fredericton Medical Society at their last monthly meeting entertained two speakers from Saint John. Dr. E. A. Petrie, radiologist of St. Joseph's Hospital, demonstrated a series of x-ray examinations indicating the usefulness of this type of examination as an aid to diagnosis. Dr. J. K. Sullivan, spoke on the diagnosis of various kidney lesions. His paper was also illustrated. Both papers elicited a large amount of discussion.

The program for the meeting of the New Brunswick Medical Society, which this year will be held in Moncton, is now completed. The profession of New Brunswick will be privileged to hear papers by Dr. Frank Lahey, Dr. Wm. P. Murphy, and Dr. Howard F. Root, all of Boston. Also on the program will be Dr. B. F. McNaughton, of Montreal, Dr. C. W. Holland, of Halifax, and Mr. James Dever, of Saint John. It is expected that at the annual luncheon of the Society the special speakers will be Dr. T. H. Leggett of Ottawa, President of the Canadian Medical Association and Dr. T. C. Routley, the General Secretary of the Canadian Medical Association.

A considerable number of New Brunswick doctors attended the meeting of the American College of Surgeons at Halifax, at which Dr. G. A. B. Addy presided as regent of the American College of Surgeons.

There has been recently a rather sharp epidemic of typhoid in rural New Brunswick, confined to one village in which there has been 14 cases of rather severe type with 3 deaths. The source of infection was traced to a broken sewer, which in connection with the spring rains polluted several dug wells. This investigation was carried out rapidly by the Public Health Department of the Province and the epidemic was quickly under control.

Military Orders in M.D. No. 7., in May, reported that Lt.-Col. R. A. Hughes had been appointed D.M.O. for the district, to succeed Lt.-Col. A. B. Walter, resigned.

A. STANLEY KIRKLAND

Nova Scotia

The meeting of the Maritime Section of the American College of Surgeons on May 20th and 21st at Halifax, drew a large attendance from the practitioners in the three Maritime provinces. Dr. J. G. MacDougall was chairman of the Committee on Local Arrangements. Several prominent members of the American College of Surgeons attended. Dr. George Crile, of Cleveland, Chairman of the Board of Regents, was present at the meetings. The clinics were exceptionally well attended.

On the evening of May 21st, a community health meeting was held in the Dalhousie gymnasium and was addressed by several of the visiting Fellows of the college. Nine topics were dealt with in short talks.

The Grace Maternity Hospital at Halifax, which has been in operation for 18 years, is appealing to the public for support. The deficit, chiefly due to the large numbers of free patients treated, is greater this year because a new heating system has been installed.

Dr. Murray MacKay, at present on the staff of the Nova Scotia Hospital, has been appointed superintendent in succession to the late Dr. J. L. Churchill.

During the absence of the premier from the province, Hon. Dr. F. R. Davis, Minister of Health, was appointed acting provincial secretary and member of the executive council.

Dr. W. W. Patton, M.P.P., retires at the end of this session from the provincial legislature and he will not seek re-election.

Applications from the Maritime provinces and Newfoundland for entrance to the first year for the study of Medicine at Dalhousie University, are greater than in any previous year. To date they are as follows: Dalhousie, 23; Mount Allison, 14; St. Francis Xavier, 12; Acadia, 2; University of New Brunswick, 2; Prince of Wales College, 2; Memorial College, 2. Applications have also been received from Saskatchewan, 4; Ontario, 2; Alberta, Quebec and Manitoba, 1 each.

The annual meetings of some medical societies in the province have been held and officers have been elected.

The Western Nova Scotia Society elected Dr. A. B. Campbell, of Bear River, *President*, and Dr. G. A. Dunn, of Pictou, was elected *President* of the Pictou Branch of the Nova Scotia Medical Society.

Dr. Enid Johnson, who graduated from Dalhousie University this year, intends to leave for India in October to undertake medical work at one of the mission stations at Chicacole.

N. B. DREYER

Ontario

Dr. Smirle Lawson, of Toronto, has been named Chief Coroner of Toronto and Supervisory Coroner for Ontario, filling the vacancy caused by the death of Dr. M. M. Crawford.

Announcement was made at the end of May that a provincial grant of $100,000 would be made towards the cost of constructing a $400,000 addition to the Toronto Hospital for Consumptives at Weston. The extension to the building will be of three storeys and will accommodate approximately 125 beds.

The Government also announced their intention of aiding in the extension of existing accommodation for the tuberculous at Windsor. The eastern sanatorium near Cornwall is practically completed. Recent newspaper announcement would indicate that the provincial government was soon to take further steps towards combating tuberculosis in Ontario.

The laboratory services of the provincial Department of Health are now undertaking the diagnosis of pneumonia from the sputum, in Toronto and in seven other centres. Serum for types one and two is available through the provincial Health Department but has not yet been placed for free distribution.

On April 30th, the new nurses' residence of the Woodstock General Hospital was opened.

On May 20th, His Excellency, the Governor-General, officially opened the new St. John's Convalescent Hospital which is on a 21-acre property at Newtonbrook, a few miles north of the City of Toronto limits. At present it can accommodate 67 patients. It is low and broad, constructed of red brick, and is three storeys high. It is so constructed that it may be the nucleus of a larger building, or group of buildings, which may be necessary to round out the cycle of Toronto institutions of that kind.

The Alumni of the Medical Faculty of the University of Western Ontario held their annual banquet on May 1st with a large attendance. The guest speaker was the Honourable, the Minister of Health for Ontario.

The medical students' loan fund has loaned over $10,000 to worthy students since its inception by Dr. L. G. Rowntree seven years ago.

Dr. Lewis Ralph Yalland, of the University of Western Ontario, 1912, and M.R.C.P., London, 1922, has been elected a Fellow of the Royal College of Physicians of London.

J. H. ELLIOTT

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Each c.c. contains the haemopoietic factor derived from 100 grams of fresh liver.

Available in 1.1 c.c. ampoules (boxes of 4)

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Quebec

The Department of Health of the City of Montreal has recently instituted a campaign to lessen the mortality in childbirth and has circularized the medical men of the province with a view to eliciting their cooperation. Also, the department is sending letters to all newly confined women, giving them good advice in regard to the proper conduct of pregnancy which may stand them in good stead for future occasions. They are requested to pass on the information to their friends. It is hoped by this means to inform women as to the dangers inherent in the pregnant state and to encourage them to consult their doctors early.

The table appended is informative.

MATERNAL MORTALITY 1929 - 1936

Rate per 1,000 live births

International Nomenclature	*Causes*	*1929*	*1930*	*1931*	*1932*	*1933*	*Average 5 years*	*1934*	*1935*	*1936*
140-141	Abortions	0.54	0.57	0.48	0.85	0.92	0.66	0.92	1.27	0.83
142	Ectopic gestation	0.20	0.33	0.19	0.40	0.11	0.25	0.54	0.05	0.36
	Total 1st group	0.74	0.90	0.67	1.25	1.03	0.91	1.46	1.32	1.19
144	Puerperal hæmorrhage	0.44	0.72	0.63	0.70	0.98	0.69	0.60	0.58	0.71
145	Puerperal septicæmia	1.27	1.48	1.40	1.40	1.19	1.35	1.46	1.04	1.37
146-147	Albuminuria & toxæmia	0.93	0.95	0.87	1.10	1.19	1.00	0.87	1.15	1.19
148	Phlegmasia alba dolens	0.24	0.42	0.19	0.20	0.26	0.27	0.22	0.11	0.36
143, 149, 150	Others	0.54	0.72	0.58	0.30	0.32	0.50	0.65	0.75	0.42
	Total 2nd group	3.42	4.29	3.67	3.70	3.94	3.81	3.80	3.63	4.05
	Grand Total	4.16	5.19	4.34	4.95	4.97	4.72	5.26	4.95	5.24

United States

Sixteenth Annual Session American Congress of Physical Therapy.—The 16th annual clinical and scientific session of the American Congress of Physical Therapy, will be held on September 20th, 21st, 22nd, 23rd and 24th, at the Netherland Plaza Hotel, Cincinnati. Physicians, their technical assistants, and nurses working in institutional departments of physical therapy are urged to attend this important session. There will be no registration fee. Richard Kovacs, New York, Secretary.

General

The Third International Week in Switzerland, organized by the *Journal Suisse de Médecine,* will be held at Interlaken, Switzerland, from August 29th to September 4th. The subjects dealt with will concern various branches of medicine but will be specially chosen to meet the needs of the general practitioner. Distinguished clinicians from London, Paris, Oxford, Zurich, Graz, Freiburg i. Br., Bâle, Berlin, Gentofte, Bordeaux and other places will deliver lectures.

All information can be obtained from *Le Journal Suisse de Médecine,* Klosterberg 27, Bâle, Switzerland.

Tenth Conference of the International Union Against Tuberculosis.—At a meeting held in Paris, with Professor Fernand Bezançon in the chair and attended by Professor Lopo de Carvalho, President of Xth Conference of the International Union Against Tuberculosis, and by Dr. Castello Branco, Secretary General of the Conference, it was decided that the latter should be held in Lisbon from September 5 to 9, 1937. The Portuguese Organizing Committee will forward to all the members of the Congress the new program of the Conference.

The discussion will be limited to three main subjects: *Biological Subject:* "Radiological aspects of the pulmonary hilum and their interpretations"; opening report by Professor Lopo de Carvalho (Portugal); *Clinical Subject:* "Primary tuberculous infection in relation to family and domestic associates"; opening report by Drs. J. Hatfield (United States) and D. A. Powell (Great Britain). Ten speakers selected in advance from a list presented by 44 countries belonging to the Union have been designated to open the discussion on each of the questions on the agenda.

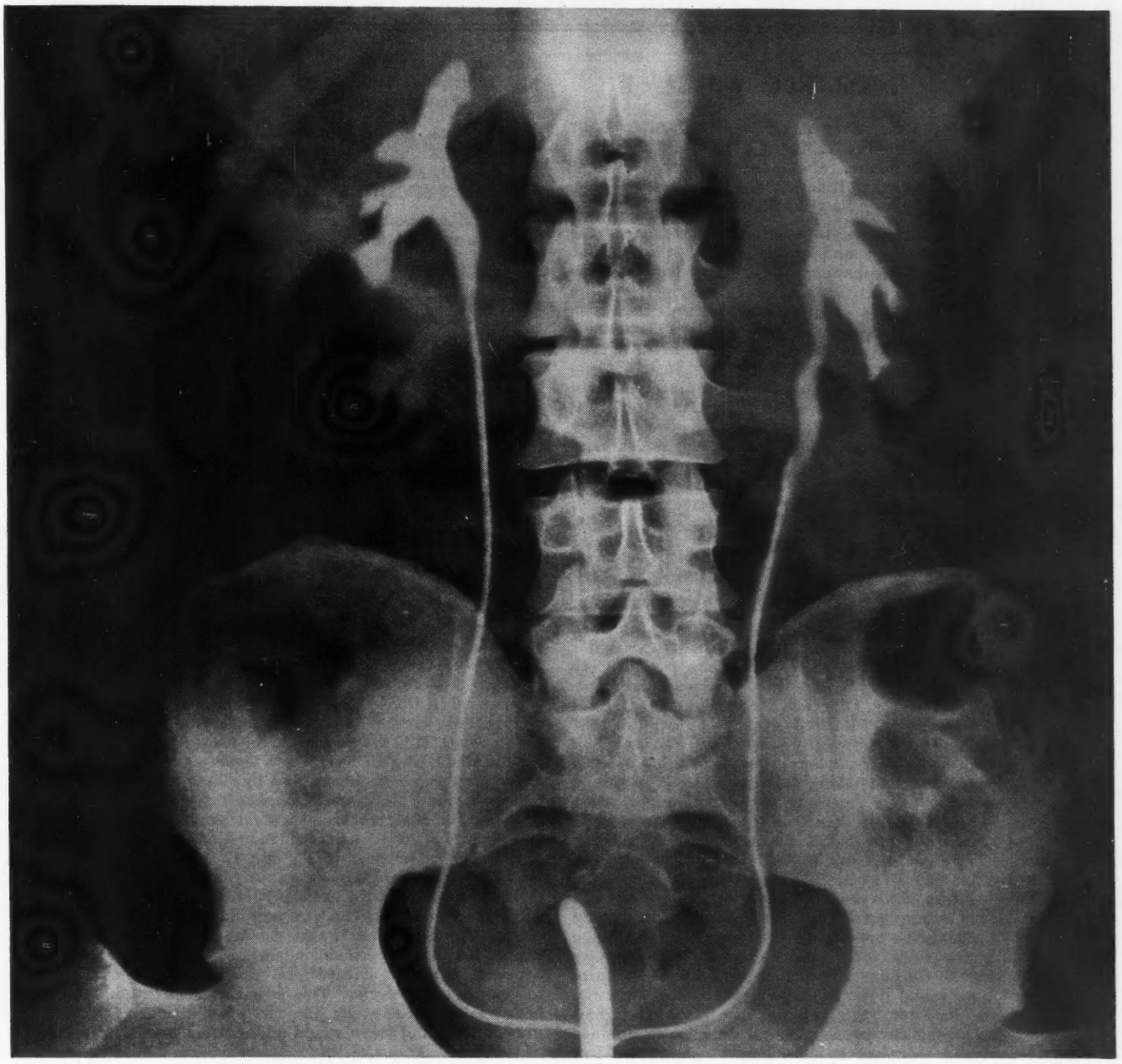
Members of the International Union may forward their application, either through the medium of their Government or their National Organization Against Tuberculosis, or directly to the Organizing Committee of the Xth Conference of the International Union Against Tuberculosis, Assistancia Nacional aos Tuberculosos, Avenida 24 de Julho, Lisbon (Portugal).

Persons who are not members of the Union and who wish to take part as "Members of the Conference" must forward their application, together with a contribution of 200 escudos exclusively through the medium of the Canadian Tuberculosis Association, 304 Plaza Building, Ottawa.

International Congress on Hepatic Insufficiency.—The International Congress on Hepatic Insufficiency, will be held in Vichy from September 16 to 18, 1937.

All applications for information, membership or subscriptions must be addressed to Dr. J. Aimard, Secretary General of the International Congress on Hepatic Insufficiency, 24, Boulevard des Capucines, Paris (IXe).

It may be stated that this Congress will be preceded by the Second International Congress on Gastro-Enterology, to take place in Paris on September 13, 14 and 15, 1937, under the presidency of Professor Pierre Duval.



40 Principal Conditions May Cause Trouble Here

THE problem of diagnosis and differentiation assumes commanding proportions when the urinary tract is involved. But efficient use of the x-ray examination has contributed mightily to the present-day accuracy with which urinary disease may be diagnosed and classified.

Simple radiography will outline the kidneys, indicating their size, shape, and position.... Pyelography will disclose calculus, sarcoma, tuberculosis, alterations in the renal pelves; also kinks in the ureter or obstructions.... Retrograde urography will demonstrate the presence of tumors, traumatisms, diverticuli, foreign bodies. In differential diagnosis, radiography will usually place the blame where it belongs.... The radiographs, by the facts that they disclose, will suggest the most effective therapeutic procedure.

For utmost assurance of accuracy in diagnosis, every sufferer from urinary disease is entitled to a thorough radiographic examination. Canadian Kodak Co., Limited, Toronto, Ontario.

RADIOGRAPHS PROVIDE DIAGNOSTIC FACTS

Book Reviews

Diseases of the Coronary Arteries and Cardiac Pain. Edited by Robert L. Levy, M.D., Professor of Clinical Medicine, Columbia University, New York. 445 pages; illustrated. Price $6.00. Macmillan Company, New York, 1936.

This book reviews to date the anatomy, physiology, pharmacology and pathology of the cardiac circulation. The mechanism of coronary pain and the clinical features, significance, and the electrocardiographic changes of coronary disease are reviewed. Sections deal with medical and surgical treatment.

The book is a comprehensive but concise survey of otherwise widely scattered material. It will probably have its greatest appeal to those interested in cardiac disease from the point of view of the internist, for it is obviously not written for the general practitioner, and to the cardiologist, most of its material will not be new. To those who have not been able to keep abreast of the growing mass of knowledge on the subject, however, the book will prove a useful and a stimulating one.

Safe Childbirth. Kathleen E. Vaughan, M.D., London. 154 pages; illustrated. Price $2.25. Baillière, Tindall & Cox, London; Macmillan, Toronto, 1937.

This book has been written with great enthusiasm and intelligence. The author becomes in it a crusader for a return to primitive life which she passionately believes would re-endow the race with a non-pathological child-bearing function. She concludes, from her observations in India, as others have done, that the difference in the function of parturition between the purdah population, where the women have little or no sunshine, no exercise, and defective diets, (although in other respects enjoying upper class amenities) and certain less privileged, but freer, river tribes who live entirely in the open, is due to the changes in pelvic form due to their respective conditions in early life; as a result, she invokes a similar contrast among western European peoples, among whom she believes the changing conditions of civilization, especially city life among the upper classes, have tended to change the optimum pelvis with equal diameters into what we are content to consider a normal pelvis—one whose brim is no longer round but whose conjugate is less than the transverse diameter. She believes that diet, habits and education among our young girls all conspire to produce an ovoid and therefore a less efficient pelvis. No less importance does she give to the rôle played by mobility of the pelvic joints and would advocate the return to the primitive squatting posture for defæcation as well as exercises designed to stretch pelvic ligaments.

Logically it follows that Dr. Vaughan advocates childbirth in what she finds, when comparing the customs of various primitive peoples, the natural postures—the squatting and crouching positions. The book maintains the above theses with a wealth of illustrations drawn from the author's extensive personal experience, and the care and sincerity with which the views are advanced enable the critical reader to overlook the frequency with which views are advanced as proven which are as yet attractive hypotheses, but only hypotheses.

There is no mention of other important biological contributing facts to dystocia, such as racial mixture and economic conditions necessitating late marriage, factors which play a large part in the problem. This book, however, will stimulate thought, especially among the conservative, and if it leads to a saner education of the growing girl so that she may approach motherhood with a more efficient body, even if the rather radical and unconvincing suggestions as to the conduct of labour are not adapted, the author will no doubt be content. Anyone who realizes the inefficiency with which man and fate have developed the reproductive function will read the book with profit.

Source Book of Orthopædics. Edgar M. Bick, M.A., M.D., Adjunct Orthopædic Surgeon, Hospital for Joint Diseases and Mt. Sinai Hospital. 376 pages. Price $4.00. Williams & Wilkins, Baltimore, 1937.

In this ambitious study Dr. Bick ably depicts the developments of orthopædic surgery from prehistoric times to the present day. The evidence of orthopædic surgery in prehistoric times is necessarily fragmentary, but with the appearance of the Hippocratic school a true appreciation of the principles of orthopædic surgery as we know it today is very clearly seen. By apt quotations from the Corpus Hippocraticum Dr. Bick depicts for us the greatness of the Father of Medicine. The accuracy of observation and the soundness of treatment in that school of medicine and in that remote age command our profound admiration. The fascinating story is continued through the middle ages and the Renaissance by the complete account of all the developments in medicine which had any bearing upon the branch of surgery we now know as orthopædics—Galen, da Vinci, Paré, all made important contributions.

In its account of the development of orthopædics from the eighteenth century on this book is a most valuable source of information. The important developments in the surgery of the extremities and of deformities are related in a manner which holds the interest to the end. It cannot fail to be a valuable source book to all who are interested in this active and rapidly growing field of surgery. Amongst so much that is commendable it is a pity to find a few grave errors. Arthrodesis of the tuberculous knee was practised by Lister when Hibbs was a child in arms (p. 244). The patella displacing incision for adequate exposure of the knee joint was first introduced by Timbrell Fisher and not by Krida (p. 278). Johansson's revolutionary contribution to the treatment of fracture of the neck of the femur (p. 185) was the introduction of a cannulated nail along a Kirschner wire guide, the position of which was accurately determined by x-ray. Kirschner's introduction of piano wire skeletal traction is deserving of more extensive comment. A section upon the development of plaster of Paris as a splinting material might well have been included. Finally, it is to be hoped that a new edition will provide an opportunity to correct two defects. This excellent monograph could be made still better by the use of judiciously chosen illustrations, and these would add greatly to the interest of the work. A new edition should certainly be published if only to correct the innumerable errors in spelling, chiefly of proper names. The proof reading of this edition has been extraordinarily lax.

The Facial Neuralgias. W. Harris, M.D., F.R.C.P., Consulting Physician to St. Mary's Hospital. 109 pages, illustrated. Price $2.50. McAinsh, Toronto, 1937.

This book represents comprehensive treatment of its subject in the Oxford Medical Publications series. As stated in the preface, "The many and baffling types of facial pain have for long appeared to me to call for a further attempt at classification and differential diagnosis". A general discussion of the wider subject "headache" is not attempted, although migraine is touched upon in connection with his so-called "migrainous neuralgia", which he considers to be "associated with vaso-motor spasm of the middle meningeal artery", with the painful impulses transmitted by recurrent meningeal branches of the fifth nerve. This question of sensory conduction is discussed in several places, the discussion of the part played by the sympathetic being particularly stimulating. The introduction offers a more formal presenta-

TETANUS

Prophylaxis

Modern practice calls for prompt administration of tetanus antitoxin in conjunction with surgical treatment of contused and puncture wounds. Depending on the extent of the injury, either 1500 units or 3000 units (3000 or 6000 international units) of this antitoxin should be given as a prophylactic. The value of this procedure is evidenced by the fact that few of the forty deaths from tetanus recorded in Canada last year resulted from injuries treated in hospitals where the procedure is followed as a matter of routine.

Recent studies have demonstrated the efficacy of tetanus toxoid in active immunization. A series of three doses of this product affords protection against tetanus comparable to the protection against diphtheria which is conferred by administration of diphtheria toxoid. This is of special interest to persons engaged in certain occupations in which the menace of tetanus is relatively great.

Treatment

In treatment of tetanus the usefulness of tetanus antitoxin has been well established. To be properly effective, however, the antitoxin must be administered as promptly as possible and in large quantities. With this in mind the tetanus antitoxin prepared in the Connaught Laboratories is most carefully refined and concentrated for use intramuscularly, intravenously and intraspinally.

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tion of the connections and functions of the 5th, 7th, 9th, and sympathetic nerves.

The main part of the book is naturally taken up with trigeminal tic. Particularly interesting are the discussions of the history and of the etiology, the condition being attributed chiefly to dental sepsis (perhaps persisting or occurring after the teeth are removed), irritating the dental branches of the nerve, with other factors such as heredity, disseminated sclerosis, basal tumours, etc. The technique of alcohol injection is given in unnecessarily great detail for a procedure which, although "minor", is delicate and requires to be learnt, not from a text-book but from observation and experience of the actual procedure. However, the general discussion of the treatment is eminently sound, as is that of the scope of and indications for injection, and after-care.

Other scattered sections discuss neuralgias associated with dental decay, ocular causes, trauma, herpes, tumours, arterial disease, sinusitis, geniculate and glossopharyngeal neuralgias. Psychogenic causes are touched upon lightly, even too lightly. The arrangement of the book perhaps does not present the clearness of an orderly picture, but the author's wide experience, broad view, and thoughtful consideration make it very useful for anyone concerned with facial pain.

Synopsis of Ano-rectal Diseases. Louis J. Hirschman, M.D., F.A.C.S. 288 pages, illustrated. Price $4.00. McAinsh, Toronto, 1937.

This volume, a synopsis of ano-rectal diseases, is the fifth edition of this work which first appeared in 1909. The book covers the commoner lesions of the anus and rectum, and many of its chapters represent the experience and personal viewpoint of the author. The subject matter is clearly written and the illustrations numerous. The author does not deal with many of the major lesions of the ano-rectum and sigmoid, and theoretical discussions and references are more or less excluded. The volume is essentially a practical manual and not a textbook; useful for those who wish to gain an elementary and general knowledge of the lesions of the terminal bowel.

The Ocular Fundus in Diagnosis and Treatment. Donald T. Atkinson, M.D., F.A.C.S., Consulting Ophthalmologist to the Santa Rosa Infirmary, San Antonio, Texas. 142 pages, illustrated. Price $10.00. Lea and Febiger, Phila., 1937.

Everyone will admit that the ocular fundus is often a finger-post pointing to the existence of general constitutional or special systemic disease. Every one will admit also that all medical men should be reasonably expert in the use of the ophthalmoscope and be conversant with at least the commoner significant changes in the eye grounds. Neurologists, obstetricians, surgeons, and diagnosticians, if attached to large hospitals, may be able to call upon the services of the eye specialist, but all are not so favourably circumstanced, and even they at times may find it more convenient to make their own ophthalmoscopic examinations. The general man, also, will at times be in the same position. But, granting that the individual practitioner is able to make his own examinations, he may not be able to interpret fully what he may see. This book will help him. Dr. Atkinson has attempted to outline for all such the general characteristics of the ocular fundus in a clear, simple and helpful manner and to indicate the practical applications of these in health and disease. He has succeeded admirably. His book is comprehensive, easily understood, and succinct. The book begins with a chapter on the ophthalmoscope and its use; then the author takes up systematically the consideration of the normal fundus, the anatomy of the retinal vessels, the optic nerve, the vitreous humour, the retina, and the choroid, in each case dealing with the changes in the fundus induced by various pathological processes. Nothing of importance seems to be omitted. The book ends with a consideration of the ordinary ophthalmoscopic manifestations in the chief special diseases. The illustrations call for special note. They represent the clinical experience of the author and certain of his colleagues, and have the added interest that they are the work of the author himself. They are altogether admirable, and the coloured pictures in particular are strikingly graphic and beautiful.

The book is not large, yet manages to convey its message adequately. It should be in the hands of every medical man.

Inhalational Anæsthesia — A Fundamental Guide. Arthur E. Guedel, M.D., Associate Clinical Professor of Surgery (Anæsthesia), University of Southern California. 163 pages. Price $2.50. Macmillan Co., New York and Toronto, 1937.

The author has provided the would-be anæsthetist with an authoritative guide to modern inhalational anæsthesia. The division of narcosis into the respective stages and planes is made very clear with the aid of diagrams, and if followed carefully should obviate any gross error in the administration of anæsthetic agents.

Considerable attention is given to anæsthetic accidents or difficulties and deaths under anæsthesia; and sound advice is given as to the best way to deal with the various complications which may occur. The question of explosibility of various anæsthetic agents is considered, which is of particular interest at the present time in view of the widespread use of cyclopropane. The author concludes that grounding of the apparatus and operating table is impracticable in application and places the greatest reliance on a high relative humidity in the operating room (60 per cent), and on routine wetting of the face mask, rubber tubing, and rebreathing bag before each induction.

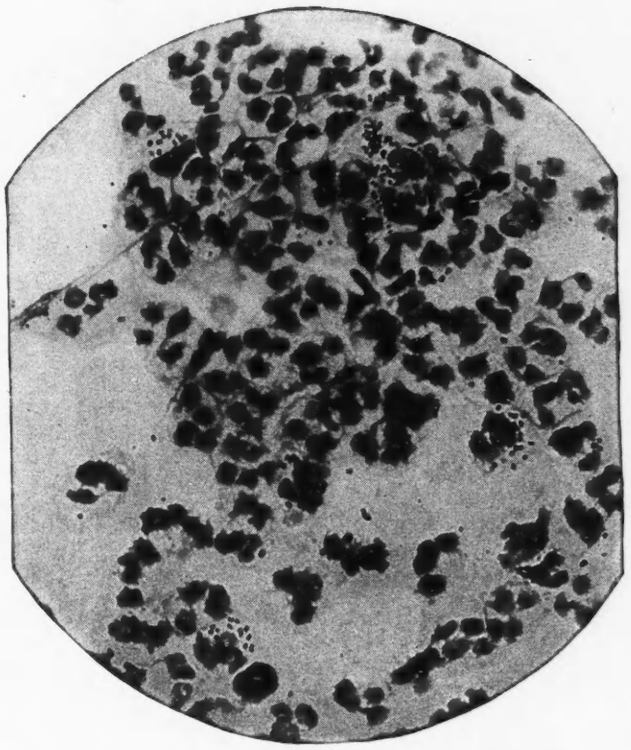
This is an acceptable contribution to the literature on anæsthesia by an outstanding authority on the subject. It is unreservedly recommended to all interested in the administration of anæsthetics.

Medical Diagnosis. S. Levy Simpson, M.A., M.D., M.R.C.P., Physician to Willesden General Hospital. 244 pages. Price 10s. 6d. Lewis, London, 1937.

The author aims high, but admits the difficulty as well as the importance of his subject. He wisely holds that the essentials of general medical diagnosis are a common meeting ground for the general practitioner and specialist. For that reason he has felt that he should try to handle the subject alone rather than have it divided amongst a number of specialists. The writing is clear and direct and a good deal of material is contained in a short compass. There is, of course, no detailed discussion, but points are suggested which can be followed up elsewhere. The entire absence of illustrations is probably the result of a choice between the extremes of none or a great many.

Nutritional Factors in Disease. William R. Fearon, M.B., Sc.D., F.I.C. 137 pages. Price $2.25. Wm. Heinemann, London; Macmillan Co., Toronto, 1936.

Interest in what to eat has been recently stimulated from very different sources. The pædiatrician wants children to grow into the perfect creatures that they might be; the militarist also desire unblemished men to bear arms. Relief committees must know how little people of different ages can eat and maintain health. A member of a western legislature recently stated in the house that fresh fruits and vegetables were a luxury. He had not heard about vitamin C.



Evidently

ALSO SPECIFIC AGAINST GONOCOCCUS

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KEEN interest has been manifested in the published observations of Drs. J. E. Dees and J. A. C. Colston (*J.A.M.A.*, 108:1855, May 29, 1937) that gonorrhea can be cured with remarkable rapidity by the use of Prontylin. The cases dealt with comprised acute, subacute and chronic anterior and posterior urethritis, inguinal adenitis, urethral stricture, seminal vesiculitis, epididymitis and prostatitis.

Judging from confirmatory publications on the value of Prontosil in gonococcus infections, as well as from numerous unpublished experiences, it would seem that a revolutionary change is impending in the treatment of another plague of humanity.

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4 tablets 4 times daily for first 2 days 3 tablets 4 times daily for next 3 days 2 tablets 4 times daily for 4 to 8 days	Total 100-132 5 grain tablets

EXCELLENT TOLERANCE: With few exceptions, the foregoing doses were tolerated without side effects. Occasionally, the initial larger doses caused slight dizziness and lassitude, and in one instance fever and sulphemoglobinemia, which disappeared when the medication was reduced or discontinued.

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This book supplied much information briefly in a clear pleasing style. Modern work on nutrition is reviewed and set forth in an orderly fashion under these headings: nature of nutrition, here the work done by the Health Organization of the League of Nations and by the Bureau of Home Economics of the United States on minimum dietary requirements is given; nutritional factors in disease, carbohydrates, proteins and lipids are discussed; the inorganic food-stuffs, calcium, phosphorus and sulphur; the inorganic micro-constituents, iron and copper; and the organic micro-constituents, the vitamins.

The information is compact, concise and modern. This is a handy reference book for the medical student, the dietitian and the practising physician.

The Fundamentals of Electrocardiographic Interpretation. J. Carter, M.D. 326 pages, illustrated. Price $4.50. Thomas, Springfield, 1937.

Essentials of Electrocardiography. R. Ashman, Ph.D. and E. Hull, M.D. 212 pages, illustrated. Price $3.50. Macmillan Co., Toronto, 1937.

These two books resemble each other so closely in aim, subject matter, arrangement and length that it is impossible to make a distinction between them. The authors of both had in mind to provide physicians generally with information, illustrated by specimen tracings, that might enable them to recognize normal electrocardiograms and to interpret the commoner abnormal ones, or at least to view an electrocardiogram with more understanding than is usually possessed by one who is not a specialist in this field. It might be pointed out that some danger attaches to attempts of the inexperienced to interpret electrocardiograms, as some reveal their true significance only to the expert. If then, the practitioner who sees only an occasional electrocardiogram is still to rely upon the specialist one might argue that it does not matter whether he knows how the interpretation is made or not. In large measure such a conclusion is justified. However, for any one who wishes to add to his knowledge either of these books will prove satisfactory in the matter of electrocardiography.

Physical Diagnosis. Ralph H. Major, Professor of Medicine, University of Kansas. 457 pages, illustrated. Price $5.50. McAinsh, Toronto, 1937.

A notable feature of this book is its use of classic descriptions. The author is fully qualified for this as he has already proved in some of his other publications. The result is refreshing and there is no question of the teaching value of such a method. The illustrations are numerous and excellent and often require no textual support. Altogether it is a manual which can be very highly recommended for the student and practitioner.

BOOKS RECEIVED

The Principles of Contraception. Joan Malleson, M.B., B.S. 160 pages. Price 4s. 6d. net. Victor Gollancz, London, 1935.

Emanotherapy. F. Howard Humphris, M.D., F.R.C.P., D.M.R.E. and Leonard Williams, M.D. 188 pages. Price $2.25. Baillière, Tindall & Cox, London; Macmillan, Toronto, 1937.

The Morphine Habit and Its Painless Treatment. G. Laughton Scott, M.R.C.S., B.A. Second ed., 105 pages. Price 5s. net. H. K. Lewis, London, 1937.

Cancer and Diet. Frederick L. Hoffman, LL.D., Biochemical Research Foundation, Franklin Institute, Philadelphia. 767 pages. Price $5.00. Williams & Wilkins, Baltimore, 1937.

Tuberculosis, Cancer and Zinc. Douglas B. Cruickshank, L.R.C.P. and S., L.D.S., D.P.H., Member of Research Staff, Papworth Village Settlement. 75 pages. Price 7s. 6d. Medical Publications, 25 Soho Square, London, 1936.

The Control of Bovine Tuberculosis in Man. Nathan Raw, C.M.G., M.D., M.R.C.P. 128 pages. Price $1.75. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1937.

History of Modern Morals. Max Hodann. Translated by Stella Browne. 338 pages. Price $3.75. Wm. Heinnemann, London; Macmillan, Toronto, 1937.

Sexual Power. Chester T. Stone, M.D., Clinical Assistant Surgeon, Urological Department, Bellevue Hospital. 172 pages. Price $1.50. D. Appleton-Century, New York and London, 1937.

Vade Mecum of Medical Treatment. W. Gordon Sears, M.D., M.R.C.P., Deputy Medical Superintendent, St. Charles' Hospital, London. 368 pages. Price $3.00. Ed. Arnold, London; Macmillan, Toronto, 1937.

Contributions to the Microscopic Anatomy of the Pancreas. Paul Langerhans. Translated by H. Morrison, M.D. 39 pages. Price $1.00. Johns Hopkins Press, Baltimore, 1937.

Physiology for Pharmaceutical Students. Harold H. Barber, B.Sc., Ph.D., F.I.C., Head of Sub-department of Physiology, University College of Nottingham. 477 pages, illustrated. Price $3.75. Baillière, Tindall & Cox, London; Macmillan, Toronto, 1937.

Medical Urology. Irvin S. Koll, B.S., M.D., F.A.C.S., Attending Urologist, Michael Reese Hospital. 431 pages, illustrated. Price $6.00. C. V. Mosby, St. Louis; McAinsh, Toronto, 1937.

Diathermy. Elkin P. Cumberbatch, M.A., B.M., D.M.R.E., F.R.C.P., Medical Officer in Charge of Electrical Dept., St. Bartholomew's School. Third ed., 576 pages, illustrated. Price $6.25. Wm. Heinemann, London; Macmillan, Toronto, 1937.

Neuroembryology. Samuel R. Detwiler, Professor of Anatomy, College of Physicians and Surgeons, Columbia University. 218 pages. Price $3.75. Macmillan Co., New York and Toronto, 1937.

The Spectacle of a Man. John Coignard. 252 pages. $2.50. Jefferson House, New York, 1937.

Classification for Medical Literature. Compiled by Eileen R. Cunningham, Librarian, Vanderbilt University School of Medicine. Second ed., 104 pages. $2.00. Cullom & Ghertner, Nashville, 1937.

International Clinics. Edited by L. Hamman, M.D. Vol. 2, forty-fifth series. 315 pages, illustrated. Price $3.00. J. B. Lippincott, Montreal, 1937.

Handbook of Hygiene. Joseph W. Bigger, M.D., Sc.D., F.R.C.P.I., D.P.H., M.R.I.A., Professor of Bacteriology and Preventive Medicine, University of Dublin. 405 pages. Price $3.00. Baillière, Tindall & Cox, London; Macmillan, Toronto, 1937.

Fluorine Intoxication. Kaj Roholm, Copenhagen. 364 pages, illustrated. Arnold Busck, Copenhagen, 1937.

Cancer — The Great Darkness. By the Editors of "Fortune". 80 pages. Price $1.00. Doubleday, Doran & Co., New York, 1937.